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Synthetic Methods of Organic Chemistry

9

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From the Prefaces to the Preceding Volumes

New methods for the synthesis of organic compounds, improvements of known methods, and also old proved methods scattered in periodicals, are being recorded continuously in this book series.

An attempt has been made to develop the system of Weygand (Organic Preparations, Interscience Publishers, Inc., New York, 1945), and to group the reactions on a simple, although purely formal, basis. This has led to the invention of reaction symbols that can be classified systematically so that the methods can be treated without knowledge of the current trivial and author names (e.g., "Oxidation" and "Friedel-Crafts reaction").

Readers accustomed to the common notations will find these in the subject index. In many cases, particularly in searching for complex reactions, use of the classification system may be avoided by consulting the subject index. It is thought that the volumes should be kept close at hand. They should provide a quick survey, and obviate the immediate need for an elaborate library search. Syntheses are therefore recorded in the subject index by starting materials and end products, along with the systematic arrangement for the methods. This makes possible a sub-classification within the reaction symbols by reagents, a further methodical criterion. Starting with Volume 5, a table indicating the sequence of the reagents has been included. It may help the reader to locate reactions in the body of the text, particularly within large chapters. This table also contains such frequently used reagents as NaOH and HCl, which are not included in the subject index. Another innovation is the indexing of complex compounds with cross references under the related simpler compounds. General terms, such as synthesis, replacement, heterocyclics, may also be brought to the special attention of the reader.

The abstracts are limited to the information needed for an appraisal of the applicability of a desired synthesis. This includes the number and nature of the reaction steps, the yield, and the important literature in question. In order to carry out a particular synthesis it is therefore still necessary to have recourse to the original papers or, at least, to an abstract journal. In order to avoid repetition, selections are made on the basis of most detailed description and best yields, whenever the same method is used in similar cases. Continuations of papers already included will not be abstracted, unless they contain

essentially new information. They may, however, be quoted at the place corresponding to the abstracted papers. These supplementary references make it possible to keep abstracts of previous volumes up-to-date.

Furthermore, to avoid a "jungle" of references, the following limitations have been decided on: Papers are not included, if their content does not fit the subject matter of "Synthetic Methods" and if they can be found easily in the indexes of the abstract journals. Less accessible and readable papers, such as the Russian or Japanese ones, are only abstracted, as a rule, if the method in question is described nowhere else. Since publications dealing with organic chemistry are increasing from year to year, some unintentional omissions may occur as well. Therefore, the editor will be grateful if important methods not yet mentioned are brought to his attention.

Syntheses that are split into their various steps, which are recorded in different places, can be followed with the help of the notations *startg. m. f.* (starting material for the preparation of ...) and *prepn. s.* (preparation, see).

Aus den Vorworten zu den vorhergehenden Bänden

In dieser Buchreihe sollen neue Methoden zur Synthese organischer Verbindungen, Verbesserungen bekannter und auch bewährte ältere Methoden, die sich in den in Fachzeitschriften veröffentlichten Originalarbeiten verstreut vorfinden, laufend registriert werden.

Aufbauend auf der Weygandschen Systematik wurde versucht, alle Reaktionen an Hand weniger einfacher, wenn auch rein formaler Richtlinien zu ordnen. Dies führte zur Ausarbeitung von Reaktions-Formelzeichen, die sich im Gegensatz zu den bisherigen Trivial- bzw. Autorennamen, wie Oxydation, Friedel-Crafts-Synthese, systematisch anordnen lassen. Man kann so die Methoden, ohne ihren Namen zu kennen, mittels des Formelzeichens auffinden.

Benutzer, die an die alten Bezeichnungen gewöhnt sind, finden diese im alphabetischen Register, das in vielen Fällen den Gebrauch der Systematik entbehrlich machen und besonders zum Aufsuchen komplizierter Reaktionen mit Vorteil benutzt werden dürfte. Da die Sammlung für die Handbibliothek am Arbeitsplatz im Laboratorium gedacht ist, soll sie eine rasche Orientierung gestatten, ohne daß fürs erste die Literatur der Instituts- oder Werkbibliothek herangezogen werden muß. Neben der systematischen Registrierung der Methoden werden deshalb im alphabetischen Register auch Synthesen durch ihre

Ausgangs- und Endprodukte registriert. Dies ermöglicht es, im Text, innerhalb der Reaktionszeichen, nach einem weiteren methodischen Kriterium, nämlich den Hilfsstoffen einzuteilen. Beginnend mit Band 5 ist eine Tafel aufgenommen worden, die die Reihenfolge der Hilfsstoffe angibt. Sie dürfte zum Aufsuchen von Reaktionen im Text, besonders in großen Kapiteln, nützlich sein. Sie enthält auch so häufig gebrauchte Hilfsstoffe wie NaOH und HCl, die im alphabetischen Register nicht aufgeführt sind. Neuartig ist ferner die Registrierung der komplizierten Verbindungen. Auf Sammelbegriffe wie Aufbau, Austausch, Heterocyclen sei noch besonders hingewiesen.

Die Referate beschränken sich auf das zur Beurteilung der Zweckmäßigkeit einer Synthese Notwendige, wie Zahl und Art der Reaktionsstufen, die Ausbeute, wichtige, die Methode betreffende Literatur usw. Vor Ausführung einer bestimmten Synthese ist es deshalb erforderlich, das chemische Zentralblatt oder ein anderes Referatenblatt und, wenn möglich, auch die Originalarbeit zu Rate zu ziehen. Zur Vermeidung von Wiederholungen wurden bei der Anwendung einer Methode in ähnlichen Fällen diejenigen ausgewählt, die am ausführlichsten beschrieben sind und die besten Ausbeuten geben. Fortsetzungen bereits aufgenommener Arbeiten, die nichts wesentlich Neues bringen, werden nicht mehr referiert, evtl. aber an der Stelle der aufgenommenen Arbeit zitiert. Diese Ergänzungszitate ermöglichen es, Referate aus früheren Bänden auf den neuesten Stand zu bringen.

Um ferner das Material nicht zu sehr auf Kosten der Uebersicht anschwellen zu lassen, werden Veröffentlichungen, die nicht ganz in den Rahmen der «Synth. Meth.» passen und die in den Sachregistern der Referatenblätter leicht aufgefunden werden können, nicht aufgenommen. Arbeiten aus schwerer zugänglichen und lesbaren Zeitschriften, wie z. B. den russischen und japanischen, werden im allgemeinen nur dann referiert, wenn die betreffende Methode sonst nirgends beschrieben ist. Da die Zahl der Veröffentlichungen auf dem Gebiete der organischen Chemie von Jahr zu Jahr zunimmt, unterbleibt die Aufnahme von Arbeiten manchmal auch unabsichtlich. Wir wären deshalb dankbar, wenn wir auf wichtige Methoden aufmerksam gemacht würden, die in unserer Sammlung noch nicht enthalten sind.

Synthesen, die in ihre Stufen zerlegt und an verschiedenen Stellen eingeordnet sind, können mit Hilfe der Vermerke *startg. m. f.* (Ausgangsmaterial für die Darstellung von ...) und *prepn. s.* (Darstellung siehe) zusammengesetzt werden.

Preface to Volume 9

Most of the abstracts in this volume are of papers published between 1952 and 1954. As Volume 8 it contains a brief review, Trends in Synthetic Organic Chemistry, stressing some highlights of general interest and calling attention to developments too recent to be included in the body of the text.

The index covers only Volume 9, as the next volume, which concludes the second series, will contain both a cumulative index and arrangement of all titles of Volumes 6 to 10.

I want to thank Dr. John T. Plati once more for having checked the manuscript and Dr. Bernhard Prijs for his thorough proof-reading. I also greatly appreciate the valuable advice they have given me. Thanks are due again to Dr. J. A. Aeschlimann, Vice President of Hoffmann-La Roche, Inc., for liberally providing me with library and office facilities.

Nutley, New Jersey, U.S.A., May 1955. W. Th.

Vorwort zu Band 9

Der vorliegende Band 9 der «Synthetischen Methoden» bringt hauptsächlich Referate von Arbeiten aus dem Jahren 1952—1954. Auch dieser Band enthält einen kurzen Ueberblick, «Trends in Synthetic Organic Chemistry», der einige der wichtigsten Fortschritte allgemeinen Interesses aufzeigt und auf neue Arbeiten hinweist, die nicht mehr in den Hauptteil des Bandes aufgenommen werden konnten.

Das Register umfaßt diesmal nur einen Band, da der nächste Band, der die zweite Serie abschließt, sowohl ein Generalregister als auch alle Titel der Bände 6—10 enthalten wird.

Nutley, New Jersey, U.S.A., im Mai 1955. W. Th.

Method of Classification

The following directions serve to explain the system of Classification.

1. Reaction Symbols.

The first part of the symbol refers to the chemical bonds formed during the reaction. These bonds appear in the reaction symbols as the symbols for the two elements that have been linked together (e.g., the bond between hydrogen and nitrogen, as HN). The order of the elements is the same as in *Chemisches Zentralblatt* and in Beilstein's *Handbuch der organischen Chemie:* H, O, N, Hal (Halogen), S, and the remaining elements (Rem). C is always placed last.

The "principle of the latest position" determines the order of the element symbols, and is used whenever possible.

The methods of obtaining a particular chemical bond are subdivided according to methods of formation. Four types are distinguished: addition (⇊), rearrangement (⤵), exchange (⇅), and elimination (⇈). The last part of the symbol refers to the bonds which are destroyed in the reaction or to a characteristic element of that part of the molecule which is eliminated.

The following simplifying stipulations facilitate the use of the reaction symbols: *(1)* The chemical bond is rigidly classified according to the structure formula without taking the reaction mechanism into consideration. *(2)* Double or triple bonds are treated as being equivalent to two or three single bonds, respectively. *(3)* Generally speaking, only stable organic compounds are taken into consideration. Intermediary compounds, such as Grignard compounds and sodiomalonic esters, and anorganic reactants, such as nitric acid, are therefore not expressed in the reaction symbols.

Examples:

see Volume II, page viii (Interscience Publishers)

Systematic Survey

see page 473

2. Reagents.

A further subdivision, not included in the reaction symbols, is made on the basis of the reagents characteristic of the reaction. The order usually follows that of the periodic system. Reagents made up of several components are arranged according to the element significant for the reaction (e.g., $KMnO_4$ under Mn, NaClO under Cl). When a constituent of the reagent goes into the products of the reaction, the remainder of the reagent, which acts as a carrier of this constituent, is the criterion for the classification; for example, phosphorus is the carrier in a chlorination with PCl_5 and sodium in a nitrosation with $NaNO_2$. A table indicating the sequence of the reagents may be found on page 477.

3. The material between the listings of the reagents is arranged with the simple examples first and the more complicated ones following.

4. When changes in more than one chemical bond occur during a reaction, as, for example, in the formation of a new ring, or if the reaction can be carried out in different ways, these reactions are introduced in several places when necessary. The main entry in such cases is placed usually according to the "principle of the latest position"; the other entries are cross-referenced back to it.

Systematik

Für die Reihenfolge der Methoden gelten folgende Richtlinien:

1. Reaktionszeichen.

Die Einteilung erfolgt zuerst nach den Bindungen, die bei einer Reaktion entstehen. Diese erscheinen im Reaktions-Formelzeichen in Gestalt ihrer beiden Elementsymbole, z. B. die Bindung zwischen Wasserstoff und Stickstoff als HN. Die Reihenfolge der Elemente ist die gleiche wie im Chemischen Zentralblatt und in Beilsteins Handbuch der organischen Chemie: H, O, N, Hal (Halogen), S, Rem (Uebrige Elemente), C steht an letzter Stelle.

Das *«Prinzip der letzten Stelle»* bestimmt die Reihenfolge der Elementsymbole und ist auch sonst nach Möglichkeit immer angewandt worden.

Die Methoden zur Herstellung einer bestimmten Bindung werden nach ihrer Bildungsweise eingeteilt. Es werden 4 Fälle unterschieden: Aufnahme ($\Downarrow$), Umlagerung ($\curvearrowright$), Austausch ($\uparrow\downarrow$) und Abgabe ($\Uparrow$).

Der letzte Teil des Reaktionszeichens gibt die Bindung an, die gelöst wird, oder ein charakteristisches Element desjenigen Molekülteils, der abgespalten wird.

Die Bildung des Reaktionszeichens wird durch folgende vereinfachende Annahmen erleichtert:

1. Die Bindungen für die Registrierung ergeben sich rein formal aus den Strukturformeln, ohne daß auf Reaktionsmechanismen Rücksicht genommen wird.
2. Doppel- und Dreifachbindungen werden 2 bzw. 3 Einfachbindungen gleichgesetzt.
3. Es werden in der Regel nur stabile organische Verbindungen berücksichtigt, Zwischenprodukte, wie z. B. Grignard-Verbindungen, Na-Malonester und anorganische Reaktionspartner, wie z. B. Salpetersäure, werden deshalb nicht zur Bildung des Reaktionszeichens herangezogen.

Beispiele

siehe Band 2, Seite VI.

Systematische Uebersicht

siehe Seite 473.

2. Hilfsstoffe.

Eine weitere Unterteilung, die im Reaktionszeichen nicht mehr zum Ausdruck kommt, wird nach den für die Reaktion charakteristischen Hilfsstoffen vorgenommen. Ihre Reihenfolge richtet sich im wesentlichen nach dem periodischen System. Hilfsstoffe, die sich aus mehreren Bestandteilen zusammensetzen, werden nach demjenigen eingeteilt, der für die Reaktion verantwortlich ist, z. B. steht $KMnO_4$ bei Mn, NaClO bei Cl. Geht ein Bestandteil des Hilfsstoffs in das Reaktionsprodukt ein, dann ist der Rest als Träger dieses Bestandteils für die Einordnung maßgebend; das ist z. B. bei einer Chlorierung mit PCl_5 Phosphor, bei einer Nitrosierung mit $NaNO_2$ Natrium. Eine Tafel der in diesem Band verwendeten Reihenfolge der Hilfsstoffe befindet sich auf Seite 477.

3. Innerhalb dieser Unterteilung sind die einzelnen Referate von einfachen zu komplizierten Beispielen fortschreitend angeordnet.

4. Treten bei einer Reaktion Veränderungen an mehreren Bindungen ein, wie z. B. bei Ringschlüssen, oder kann sie auf verschiedene Art durchgeführt werden, dann wird sie, falls notwendig an mehreren Stellen eingeordnet. Das Hauptzitat steht in diesen Fällen in der Regel an der letzten Stelle; an den übrigen Stellen befinden sich Hinweise auf dieses.

Trends
in Synthetic Organic Chemistry
1955

For a number of years, new catalytic high pressure and temperature syntheses have been developed by Reppe et al. (cf. Synth. Meth. *3*, 588) who used acetylene and carbon monoxide as their principal starting materials. We do not intend to repeat the contents of several comprehensive publications on the subject[1]. More processes of this type, however, will eventually find their way into the current literature, and from there into future volumes of Synthetic Methods. In this connection, we mention the addition of HCN to unactivated carbon-carbon double bonds[2], and the preparation of formamides with carbon monoxide[3].

Whereas Reppe chemistry is essentially concerned with one-step syntheses of relatively simple compounds, which, in turn, can be used as building blocks for polymers, Woodward et al. have mastered multistep syntheses of highly intricate compounds. To the synthesis of quinine, patuline, and the total synthesis of the steroid skeleton, they have recently added a 30-step synthesis of the strychnine molecule[4], which has long engaged the efforts of many investigators. The total synthesis of lysergic acid in 14 steps has been carried out by a group of the Lilly Research Laboratories[5]. The synthesis of morphine by Gates and Tschudi[6] should also be mentioned at this point. The total steroid synthesis is attracting the attention of several industrial laboratories[7]. An improved oxidation method for obtaining the 17α-hydroxy-20-keto group of the cortisone side chain[8] is a result of these experiments. A number of publications deals with ergosterol as a

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[1] W. Reppe, Chemie und Technik der Acetylen-Druck-Reaktionen, Verlag Chemie, Weinheim, 1951; A. *560,* 1 (1948) and following papers; J. W. Copenhaver and M. H. Bigelow, Acetylene and Carbon Monoxide Chemistry, Reinhold, New York, 1949.

[2] P. Arthur, J., et al., Am. Soc. *76,* 5364 (1954).

[3] H. Winteler, A. Bieler, and A. Guyer, Helv. *37,* 2370 (1954).

[4] R. B. Woodward et al., Am. Soc. *76,* 4749 (1954).

[5] E. C. Kornfeld et al., Am. Soc. *76,* 5256 (1954).

[6] M. Gates and G. Tschudi, Am. Soc. *74,* 1109 (1952).

[7] e. g. Helv. *36,* 1803 (1953); Am. Soc. *76,* 1715 (1954); Am. Soc. *76,* 5011, 5014 (1954).

[8] G. I. Poos et al., Am. Soc. *76,* 5031 (1954); R. Tull et al., Am. Soc. *77,* 196 (1955).

starting material for a partial synthesis of hormones involving side chain degradation [9].

The arsenal of peptide chemistry has been further enriched by a variety of new methods including the use of phosphorus compounds such as the so-called phosphazo compounds (*9*, 468), phosphite amides (*9*, 543), and pyrophosphites as intermediates. Pyrophosphites have been used in the total synthesis of polypeptides such as oxytocin (*9*, 464), the first natural polypeptide to be synthesized. Recently, activated esters have been introduced as promising acylating agents in peptide chemistry [10]. An interesting application of the Smith reaction in this field is the conversion of subst. acetoacetic esters to α-amino esters [11]. N-Trifluoroacetyl derivatives may prove helpful in peptide chemistry because they are readily cleaved in alkaline media without damage being done to the peptide bond [12]. Carbodiimides can be employed in both the synthesis [13] and the degradation (*9*, 277) of peptides.

Protecting or blocking operations hitherto essentially confined to functional groups have been extended to the carbon skeleton itself by the use of *tert*-butyl as a blocking group. This group, of all alkyls, is exceptionally easy to remove from aromatic rings [14]. Preferential blocking of keto groups may be achieved by interchange with dioxolanes where direct ketalization is unsuccessful [15]. A mild two-step procedure for preparing phthalimides to protect sensitive *prim.* amines [16] and O-alkylation of phenolic N-bases without quaternization [17] have been described by Baker et al. In this connection, the temporary modification of a molecule as a means of boosting its reactivity may be mentioned such as the attachment of oxygen to amine-nitrogen to form the more reactive N-oxides [18].

Transfer-hydrogenation [19] with palladium as catalyst and cyclohexene as hydrogen donor is often remarkably selective and may give

[9] see D. A. Shepherd et al., Am. Soc. *77,* 1212 (1955).

[10] R. Schwyzer, M. Feurer, and B. Iselin, Helv. *38,* 83 (1955).

[11] D. O. Holland and J. H. C. Nayler, Soc. *1953,* 280.

[12] F. Weygand and M. Reiher, B. *88,* 26 (1955).

[13] J. C. Sheehan and G. P. Hess, Am. Soc. *77,* 1067 (1955).

[14] M. J. Schlatter, Am. Soc. *76,* 4952 (1954); M. Kulka, Am. Soc. *76,* 5469 (1954).

[15] Synth. Meth. *9,* 352; F. Sondheimer, M. Velasco, and G. Rosenkranz, Am. Soc. *77,* 192 (1955).

[16] B. R. Baker et al., J. Org. Chem. *19,* 1786 (1954).

[17] B. R. Baker and F. J. McEvoy, J. Org. Chem. *20,* 118, 136 (1955).

[18] Synth. Meth. *6,* 389; *8,* 260; *9,* 243; E. C. Taylor, Jr., and A. J. Crovetti. J. Org. Chem. *19,* 1633 (1954); R. Adams and S. Miyano, Am. Soc. *76,* 3168 (1954).

[19] E. A. Braude, R. P. Linstead et al., Soc. *1954,* 3578, 3586, 3595; s. a. Y. Ahmad and D. H. Hey, Soc. *1954,* 4516.

higher yields than direct catalytic hydrogenation or other methods of reduction. Phenolic hydroxyl groups may be removed by reducing the corresponding phosphoric esters with sodium or lithium in liquid ammonia [20]. Reductions with metal hydrides have been performed to advantage in pyridine, which has been used with $LiAlH_4$ to obtain methylamines from formamides [21], and with $NaBH_4$ in the preferential reduction of steroid 3-keto to 3α-hydroxy groups [22]. Two new routes from acid derivatives to aldehydes have been found: the reduction of N-methylanilides by $LiAlH_4$ [23], which can also lead to the formation of hydroxymethyl compounds, and, recently, the reduction of amidines and imidazolines with sodium and ethanol in liquid ammonia as carried out by Birch [24].

Aromatic aldehydes and alkyl aryl ketones can be synthesized by the reaction of diazonium salts with oximes (*9*, 868). Mannich bases may be converted into the corresponding aldehydes via nitrones (*9*, 553) or, directly, with hexamethylenetetramine [25]. N-Bromoacetamide has proved highly selective in the oxidation of certain *sec*. hydroxyl groups, e.g. at the 3 position of steroids [26]. Another way of achieving this oxidation is by catalytic dehydrogenation with platinum and either oxygen or air [27]. Bachmann et al. convert *prim*. amines into oxo compounds through N-chloramines and particularly recommend *tert*-butyl hypochlorite for N-chlorination [28]. Baumgarten and Bower have found a simple preparation of α-aminoketones starting from *sec*. alkylamines and rearranging the corresponding N,N-dichloroamines [29]. There is also a convenient new procedure for regenerating oxo compounds from their 2,4-dinitrophenylhydrazones [30], derivatives used most frequently for purposes of isolation and characterization.

Alkali sensitive and slow reacting α-diazoketones can be converted successfully into acids and esters by irradiation [31]. N-Methyl-N-cyano-

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[20] G. W. Kenner and N. R. Williams, Soc. *1955*, 522.

[21] B. R. Baker, R. E. Schaub, and J. P. Joseph, J. Org. Chem. *19*, 638 (1954).

[22] O. Mancera et al., Am. Soc. 75, 1286 (1953); A. J. Lemin and C. Djerassi, Am. Soc. *76*, 5672 (1954).

[23] F. Weygand et al., Ang. Ch. *65*, 525 (1953); B. *88*, 301 (1955).

[24] A. J. Birch, J. Cymerman-Craig, and M. Slaytor, Chem. and Ind. *1954*, 1559.

[25] *9*, 290; s. a. M. M. and B. L. Robison, Am. Soc. *77*, 457 (1955).

[26] R. E. Jones and F. W. Kocher, Am. Soc. *76*, 3682 (1954).

[27] R. P. A. Sneeden and R. B. Turner, Am. Soc. 77, 190 (1955).

[28] W. E. Bachmann, M. P. Cava, and A. S. Dreiding, Am. Soc. *76*, 5554 (1954).

[29] H. E. Baumgarten and F. A. Bower, Am. Soc. *76*, 4561 (1954).

[30] J. Demaecker and R. H. Martin, Nature *173*, 266 (1954); s. a. J. J. Beereboom and C. Djerassi, J. Org. Chem. *19*, 1196 (1954).

[31] Synth. Meth. *8*, 919/20; A. Roedig and H. Lunk, B. *87*, 971 (1954).

aniline has been recommended for the introduction of cyano groups (*9*, 865).

Previously inaccessible hydroperoxides may be obtained from mesylates (*9*, 166).

There are several new methods of achieving N-alkylation: Acylamines may be reduced with $LiAlH_4$ [21] (*9*, 113) or $LiBH_4$ [32]. Methylamines, in particular, can be obtained by $LiAlH_4$-reduction of urethans [33] or isocyanates (*8*, 95). Gerrard and Jeacocke [34] obtain subst. anilines by the pyrolysis of anilinophosphates. Selective N-alkylation, especially of amido groups, can be performed in acetone in the presence of KOH.

Chloral has been recommended for the formylation of strong organic bases (*9*, 545).

A new and stable reagent for making diazomethane, p-toluenesulfonylmethylnitrosamide [35], is already commercially available.

Continuing their work with phosphites, Rydon et al. have published an even simpler method of obtaining halides from alcohols [36]. Polyphosphoric acid, this very versatile reagent, makes possible the direct conversion of acids to α-bromoacids [37]. Diiodoacetylene has been recommended for the preparation of iodides [38].

A new synthesis of thiophenols using 2,4-dinitrobenzenesulfonyl chloride for the introduction of SH-groups into aromatic nuclei has been found [39]. S-Thiocarbonic acid esters proved to be convenient intermediates for the preparation of ureas, acylureas, and semicarbazides (*9*, 536). Stabilized liquid SO_3, e.g. the commercially available Sulfan, is a promising reagent for sulfonations and sulfations [40].

In the Friedel-Crafts ketone synthesis, elimination of HCl by a stream of air has been suggested [41]. In specific instances, $TiCl_4$ may be preferable to $AlCl_3$ [42]. The alkylation and acylation of ketones via enamines may be applied to compounds with base sensitive groups (*9*, 912). Amino acids are recommended as catalysts in the Knoevenagel

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[32] M. Bory and C. Mentzer, Bl. *1953,* 814.

[33] Synth. Meth. *8*, 95; R. L. Dannley, M. Lukin, and J. Shapiro, J. Org. Chem. *20,* 92 (1955).

[34] W. Gerrard and G. J. Jeacocke, Chem. & Ind. *1954,* 1538.

[35] T. J. de Boer and H. J. Backer, Org. Synth. *34,* 96, 24 (1954); R. *73,* 229, 589 (1954).

[36] D. G. Coe, S. R. Landauer, and H. N. Rydon, Soc. *1954,* 2281.

[37] E. E. Smissman, Am. Soc. *76,* 5805 (1954).

[38] V. Franzen, B. *87,* 1148 (1954).

[39] N. Kharasch and R. Swidler, J. Org. Chem. *19,* 1704 (1954).

[40] E. E. Gilbert et al., Ind. Eng. Chem. *45,* 2065 (1953).

[41] F. Smeets and J. Verhulst, Bl. Soc. chim. Belg. *61,* 694 (1952).

[42] Synth. Meth. *7,* 800; Soc. *1954,* 2942.

condensation[43]. One advantage is that they facilitate the isolation of the product. Intermolecular ring closure can be achieved without using the high dilution technique ordinarily required when polycondensation is inhibited by steric hindrance (*9*, 513). The use of trichloroacetic esters opens up a new way of synthesizing 3-subst. 2-oxazolidones and related heterocyclics[44].

Braude et al. tested 11 quinones as dehydrogenation agents and found dicyanoquinone rather than chloranil to be the most effective[45].

Dehydrations have been carried out with carbodiimides (*9*, 184), already mentioned as reagents in peptide chemistry. Sulfonic acid anhydrides[46] and nucleotides[47] have thus been made readily available. Methoxyacetylene has also been used for dehydrations (*9*, 261). Alkoxyacetylenes[48], in general, are among the more interesting compounds that recently appeared in the literature. Here are a few others: *tert*-Nitroparaffins[49], 2,4,6-tri-*tert*-butylphenoxyl[50], a stable oxygen radical, tritium-labeled compounds[51], non-classical aromatic compounds, the best known of which are the ferrocenes[52], and diketene, which has been the subject of a series of papers[53].

Ethylene oxide is a suitable means of removing hydrogen halides[54].

Resins have been used successfully as reagents by Billimoria and Maclagan[55]. In addition to hydrating the carbon-carbon triple bond with a mercury resin, as was done by Newman (*9*, 102), they hydrolyze α-ketobromides with a basic ion-exchange resin. Dowex-50 has been used to remove sodium from a liquid ammonia solution (*9*, 42). Nucleotides have been hydrolyzed with Dowex-50-H^+[56].

Future developments will show whether electric discharge as a means of gently initiating reactions will find wider application. *9*, 198 illustrates its use in the preparation of phenol from benzene.

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[43] F. S. Prout, J. Org. Chem. *18*, 928 (1953).
[44] G. Y. Lesher and A. R. Surrey, Am. Soc. *77*, 636 (1955).
[45] E. A. Braude, A. G. Brook, and R. P. Linstead, Soc. *1954*, 5369.
[46] Synth. Meth. *9*, 177; s. a. index.
[47] R. H. Hall and H. G. Khorana, Am. Soc. *76*, 5056 (1954).
[48] G. Eglinton et al., Soc. *1954*, 1860; Org Synth. *34*, 46 (1954).
[49] N. Kornblum and R. J. Clutter, Am. Soc. *76*, 4494 (1954).
[50] C. D. Cook and R. C. Woodworth, Am. Soc. *75*, 6243 (1953); E. Müller and K. Ley, B. *87*, 922, 1605 (1954).
[51] N. H. Smith, K. E. Wilzbach, and W. G. Brown, Am. Soc. *77*, 1033 (1955).
[52] cf. G. D. Broadhead and P. L. Pauson, Soc. *1955*, 367.
[53] Synth. Meth. *9*, 954; Soc. *1954*, 832, 845.
[54] Synth. Meth. *9*, 994; cf. Am. Soc. *77*, 704 (1955).
[55] J. D. Billimoria and N. F. Maclagan, Soc. *1954*, 3257.
[56] J. X. Khym, D. G. Doherty, and W. E. Cohn, Am. Soc. *76*, 5523 (1954).

The following references, contained in Vol. 8 under Trends, have been entered in this volume [57]:

4/741; 6/454; 7/452; 8/276; 9/686, 707, 718; 10/169; 11/302; 12/202; 13/735, 737; 14/881; 15/24; 16/44; 17/655; 20/63, 65, 87 a, 112; 21/87; 22/86; 24/363; 27/615; 28/846; 33/749; 34/24; 35/520; 36/968; 37/163; 38/574; 39/897; 40/533.

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[57] The first figure refers to the footnote in Trends, Vol. 8, the second figure to the entry number in this volume.

Formation of H—O Bond

Uptake

Addition to Oxygen — HO ⇓ OO

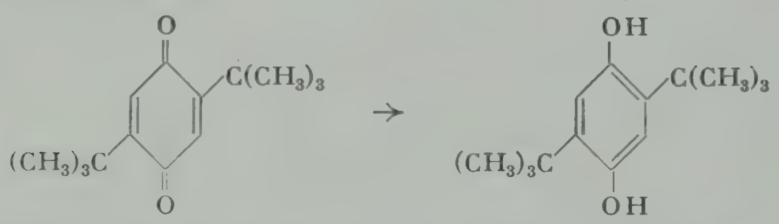
Lithium aluminum hydride — *$LiAlH_4$*

Diols from peroxides
s. *9*, 6

Addition to Oxygen and Carbon — HO ⇓ OC

Zinc/acetic acid — *Zn/CH_3COOH*

Quinols from quinones ←

1.


2,5-Di-t-butylquinone refluxed with excess Zn-dust and 80%-acetic acid → 2,5-di-t-butylhydroquinone. Y: 95%. H. M. Crawford, M. Lumpkin, and M. McDonald, Am. Soc. *74*, 4087 (1952).

Lithium aluminum hydride — *$LiAlH_4$*

2-Acylamino-3-aryl-2-propen-1-ols from azlactones
Reductive oxazolone ring opening

2.


2-Phenyl-4-(p-methoxybenzylidene)oxazolone allowed to react with $LiAlH_4$ in tetrahydrofuran at —65 to —35° → 2-benzoylamino-3-(p-methoxyphenyl)-2-propen-1-ol.—The lower temp. is maintained until the reactants are mixed. Y: 81%. F. e. s. E. Baltazzi and R. Robinson, Chem. and Ind. *1953*, 541.

Hydrosulfite — *$S_2O_4^{--}$*

Quinols from quinones ←
s. 5, 3; s. a. G. A. Reynolds and J. A. VanAllan, Org. Synth. *34*, 1 (1954)

Sulfuric acid *H_2SO_4*

Glycols from oxido compounds C—C(—O—) → C(OH)C(OH)

s. *2*, 151; s. a. R. H. Eastman and J. C. Selover, Am. Soc. *76*, 4118 (1954)

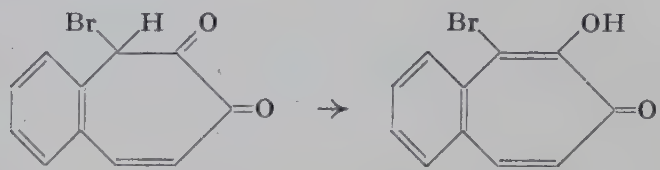
Rearrangement

Oxygen/Carbon Type **HO⤺OC**

Without additional reagents *w.a.r.*

Tropolones by enolization CHCO → C:C(OH)

3.

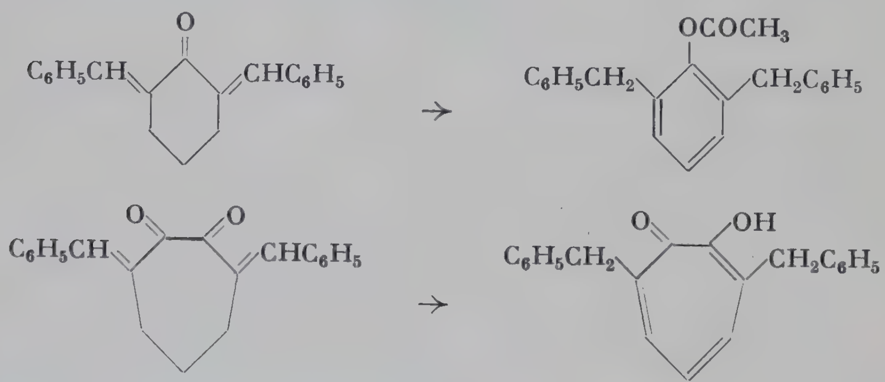


3-Bromo-4,5-benzocyclohepta-4,6-diene-1,2-dione heated at 90-95° → 3-bromo-4,5-benzotropolone. Y: ca. 100%. H. Fernholz, E. Hartwig, and J. C. Salfeld, A. *576*, 131 (1952).

Hydrobromic acid *HBr*

Phenol acetates from dienones ←
Tropolones from cyclic diene-α-diones

4.



A mixture of glacial acetic acid satd. with HBr, acetic anhydride, and 2,6-dibenzylidenecyclohexanone heated 12 hrs. at 70° → 2,6-dibenzylphenyl acetate. Y: 84%.

3,7-Dibenzylidene-1,2-cycloheptanedione and a little benzoyl peroxide added to glacial acetic acid satd. at 30° with HBr, and heated 11 hrs. at 60° → crude 3,7-dibenzyltropolone. Y: 46%.—If the benzoyl peroxide is omitted, the crude product is less readily purified. N. J. Leonard and G. C. Robinson. Am. Soc. *75*, 2143 (1953); cf. Synth. Meth. *9*, 5.

Palladium-carbon *Pd-C*

Tropolones from cyclic diene-α-diones

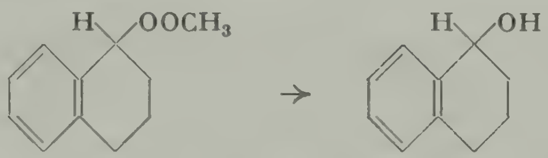
5. The use of Pd-on-charcoal as catalyst and triethylene glycol as solvent gives higher yields and is a more general method than the use of HBr/acetic acid (cf. Synth. Meth. *9*, 4).—E: 3.7-Dibenzylidene-1,2-cycloheptanedione → 3,7-dibenzyltropolone. Y: 90%. F. e. s. N. J. Leonard and J. W. Berry, Am. Soc. *75*, 4989 (1953).

Exchange

Oxygen ↑ HO ⇅ Ó

Lithium aluminum hydride *$LiAlH_4$*

Alcohols from alkyl- and acyl peroxides ←
Diols from photoöxides

6.


Dibenzoyl peroxide in dry ether added slowly with stirring to $LiAlH_4$ in ether, and refluxed 30 min. → benzyl alcohol. Y: 87.5%.—Similarly: Methyl α-tetralyl peroxide refluxed 2.5 hrs. → crude α-tetralol. Y: 95%. F. e. s. M. Matic and D. A. Sutton, Soc. *1952*, 2679; s. a. G. A. Russell, Am. Soc. *75*, 5011 (1953); diols from cyclic peroxides, in particular, s. A. Mustafa, Soc. *1952*, 2435.

Nitrogen ↑ HO ⇅ N

Sodium sulfide *Na_2S*

Cleavage of carbohydrate nitrates $ONO_2 \rightarrow OH$

7. A soln. of methyl 2-methyl-4,6-propylidene-α-D-glucoside 3-nitrate in alcohol treated with Na_2S at room temp. for 24 hrs. → methyl 2-methyl-4,6-propylidene-α-D-glucoside. Y: 78%. E. G. Ansell and J. Honeyman, Soc. *1952*, 2778.

Halogen ↑ HO ⇅ Hal

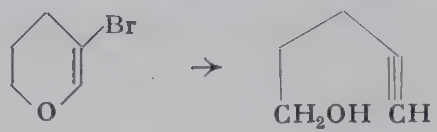
Sodium *Na*

Ethylenealcohols from cyclic halogenoethers ⊂

s. *6*, 6; introduction of isoprene units s. W. E. Parham and H. E. Holmquist, Am. Soc. *76*, 1173 (1954); prim. enynols s. O. Riobè. C. r. *236*, 2073 (1953)

Butylsodium *C_4H_9Na*

Acetylenealcohols from cyclic halogenoethers C

8. 

3-Bromodihydropyran in petroleum ether added in one portion at 0° to butyl-Na prepared from butyl chloride and Na in the same solvent in the presence of a little 1-butanol, and stirring continued 2.5 hrs. with occasional cooling → 4-pentyn-1-ol. Y: 87%. F. e. s. R. Paul and S. Tchelitcheff, Bl. *1952*, 808.

Sodium amide *$NaNH_2$*

9. 

Tetrahydrofurfuryl chloride added with stirring during 25-30 min. to $NaNH_2$, prepared from Na and liq. NH_3 in the presence of $Fe(NO_3)_3$, and stirring continued for 1 hr. → 4-pentyn-1-ol. Y: 75-85%. E. R. H. Jones, G. Eglinton, and M. C. Whiting, Org. Synth. *33*, 68 (1953).

Sodium sulfite *Na_2SO_3*

Sulfinic acids from sulfonic acid chlorides $SO_2Cl \rightarrow SO_2H$

s. *2*, 5, 581; aliphatic sulfinic acids as Mg-salts s. H. Bredereck and E. Bäder, B. *87*, 129 (1954)

Sulfur ↑ HO⇅S

Sodium amalgam *Na, Hg*

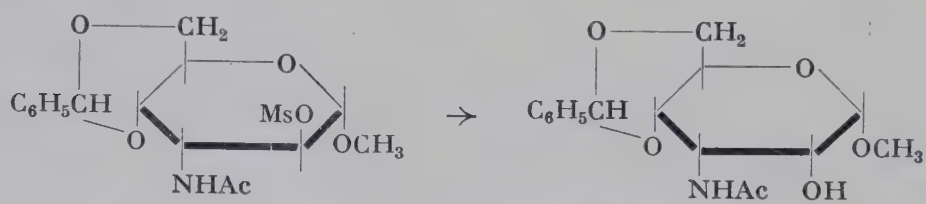
Detosylation OTs → OH

s. *2*, 6; *4*, 4; s. a. P. J. Stoffyn and R. W. Jeanloz, Am. Soc. *76*, 563 (1954)

Sodium acetate *CH_3COONa*

Demesylation $OSO_2CH_3 \rightarrow OH$

Walden inversion of acylaminosugars

10. 

A soln. of methyl 2-mesyl-3-acetamino-4,6-benzylidene-α-D-altropyranoside and anhydrous Na-acetate in 95%-ethanol refluxed 22 hrs. during

which Na-mesylate separates → methyl 3-acetamino-4,6-benzylidene-α-D-allopyranoside. Y: 79% based on startg. m. consumed.—Inversion of the 2-hydroxy analog with $SOCl_2$ was not successful. F. e., also inversion of two mesoxy groups in 95%-Methyl Cellosolve, s. B. R. Baker and R. E. Schaub, J. Org. Chem. *19*, 646 (1954).

Sulfuric acid *H_2SO_4*

Hydrolysis of sulfuric acid esters $OSO_3^- \rightarrow OH$

s. *9*, 176

Hydrochloric acid *HCl*

s. *9*, 203

Carbon ↑ HO⇅C

Sodium hydroxide *NaOH*

Hydroxymethylene compounds from alkoxymethylene compounds C:CHOR → C:CHOH

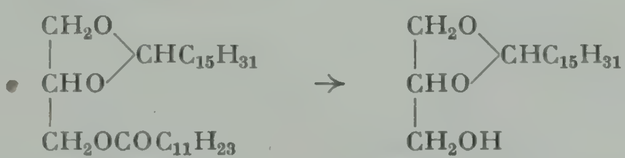
s. *5*, 5; s. a. H. Behringer and H. Weissauer. B. *85*, 774 (1952)

Deacetylation OAc → OH

s. *7*, 129; *8*, 165; s. a. W. R. Brasen and C. R. Hauser, Org. Synth. *34*, 58 (1954)

Hydroxyacetals from acoxyacetals OAc → OH
Protection of hydroxyl groups

11.



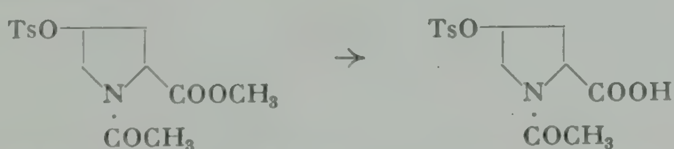
1.2-O-Hexadecylidene-3-monolaurin refluxed 6 hrs. with ethanol containing NaOH → 1.2-O-hexadecylideneglycerol. Y: ca. 100%.—Protection of the hydroxyl group by acetyl or benzoyl in place of lauroyl was not so satisfactory. M. J. Egerton and T. Malkin. Soc. *1953*, 2800.

Carboxylic acids from carboxylic acid esters COOR → COOH

s. *9*, 44

Selective hydrolysis

12.



N NaOH soln. added at 0° to a soln. of N-acetyl-O-toluenesulfonylallohydroxy-DL-proline methyl ester in methanol, and the mixture kept 18 hrs. at 0° → N-acetyl-O-toluenesulfonylallohydroxy-DL-proline. Y: 90%. R. Gaudry and C. Godin, Am. Soc. *76*, 139 (1954).

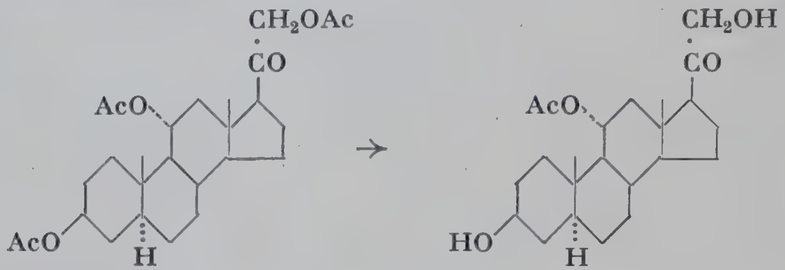
N-Carbalkoxypeptides from N-carbalkoxypeptide esters

s. *8*, 6; s. a. D. T. Gish and F. H. Carpenter, Am. Soc. *75*, 5872 (1953); E. Sondheimer and R. W. Holley, Am. Soc. *76*, 2816 (1954)

Potassium hydroxide *KOH*

Partial deacetylation of steroids OAc → OH

13.



A soln. of KOH in methanol-water added to an ice-cooled soln. of allopregnane-3β,11α,21-triol-20-one triacetate in methanol under N_2, and the product isolated after 1 hr. at room temp. → allopregnane-3β,11α,21-triol-20-one 11-monoacetate. Y: 78%. F. e. s. F. Sondheimer et al., Am. Soc. *75*, 2601 (1953).

Carboxylic acids from carboxylic acid esters COOR → COOH

s. *9*, 159

Polycarboxylic acids from polycarboxylic acid esters
Mild hydrolysis

14. $(C_2H_5OOC)_2CHCH_2CH_2CH(COOC_2H_5)_2 \rightarrow (HOOC)_2CHCH_2CH_2CH(COOH)_2$

Tetraethyl butane-1,1,4,4-tetracarboxylate shaken 12 hrs. with aq. KOH, concentrated under reduced pressure, acidified with HCl, evaporated to dryness in vacuo below 40°, and continuously extracted with ether for 2 days → butane-1,1,4,4-tetracarboxylic acid (startg. m. f. 982). Y: 95%. F. e. s. L. Crombie, J. E. H. Hancock, and R. P. Linstead, Soc. *1953*, 3496.

Potassium hydroxide/alcohol

Hydroxymercaptals from acoxymercaptals OAc → OH
Selective hydrolysis

15.

A soln. of Δ^4-cholestene-2α-ol-3-one acetate ethylenethioketal in methanol containing KOH refluxed 1 hr. → Δ^4-cholestene-2α-ol-3-one ethylene-

thioketal. Y: 73%. L. F. Fieser and M. A. Romero, Am. Soc. 75, 4716 (1953).

α-Hydroxyketones from 1-acoxy-1,2-oxido compounds ←

s. *9*, 202

Carboxylic acids from carboxylic acid esters COOR → COOH

s. *9*, 892

Sodium/alcohol *NaOR*

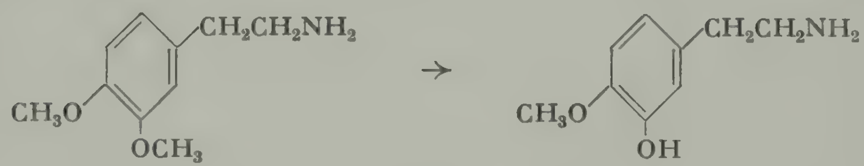
Deacetylation of carbohydrates OAc → OH

s. *9*, 229

Sodium/liq. ammonia *Na/NH₃*

Partial cleavage of methyl ethers ROR → ROH

16.



3.4-Dimethoxyphenethylamine added slowly to a soln. of Na in liq. NH_3, the mixture allowed to stand for 6 hrs. until it reaches room temp., then decomposed by cautious addition of ice → 3-hydroxy-4-methoxyphenethylamine. Y: 85%. K. E. Hamlin and F. E. Fischer, Am. Soc. 75, 5119 (1953).

Sodium carbonate *Na_2CO_3*

Partial O-deacetylation OAc → OH

s. *9*, 267

Potassium carbonate *K_2CO_3*

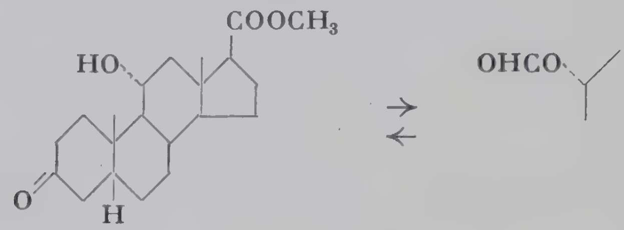
Partial hydrolysis
Deacetylation

s. *4*, 11; mandelates from acetylmandelates s. V. Prelog and H. L. Meier, Helv. *36*, 320 (1953)

Potassium hydrogen carbonate *$KHCO_3$*

Masking of hydroxyl groups
Selective hydrolysis of formoxy compounds

17.



Formates can easily be hydrolyzed and often crystallize better than acetates.—E: 95 mg. methyl 3-keto-11α-formoxyetianate (from the hydroxy compound with 99%-formic acid and acetic anhydride in pyridine) allowed to stand 3 days at 20° with $KHCO_3$ in methanol-water → 79 mg. methyl 3-keto-11α-hydroxyetianate. F. e. s. F. Reber, A. Lardon, and T. Reichstein, Helv. *37*, 45 (1954); use of trifluoroacetyl derivates s. Helv. *37*, 388.

Lithium chloride *LiCl*

Monodealkylation of phosphoric acid esters ←

s. *7*, 18; s. a. Soc. *1954*, 2381

Triton B ←

Carboxylic acids from carboxylic acid esters COOR → COOH
Cinnamylidenemalonic acids

s. *9*, 828

Barium hydroxide *$Ba(OH)_2$*

Partial hydrolysis of phosphoric acid esters ←

s. *9*, 189

Lithium aluminum hydride *$LiAlH_4$*

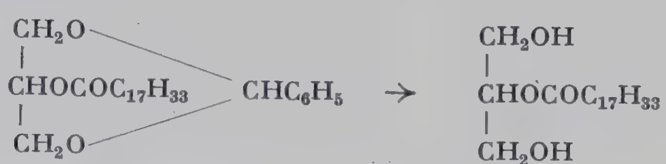
Deacylation OAc → OH

s. *7*, 20; s. a. W. A. Bonner and C. J. Collins, Am. Soc. *75*, 5372 (1953)

Boric acid *HBO_2*

Selective hydrolysis ←
Monoglycerides

18.



1,3-Benzylidene-2-elaidylglycerol dissolved in triethyl borate, finely powdered boric acid added, heated 3-5 min. at 100° until dissolved, most

of the solvent evaporated in vacuo (2-5 mm.), heating in vacuo at 100° continued for 10 min., cooled, the resulting boric acid ester dissolved in ether, and hydrolyzed by washing with water → 2-monoelaidin. Y: 86%. F. e., also isomerization to 1-monoglycerides, s. J. B. Martin, Am. Soc. 75, 5482 (1953).

Yeast ←

Disaccharides from trisaccharides ←

19. An aq. soln. of raffinose pentahydrate treated with Ca-carbonate and a nutrient soln. containing Na-nitrate, Mg-sulfate, and KH_2PO_4, baker's yeast added, kept 4 days at 37°, then worked up using ion-exchange resins → α-melibiose. Y: 88%. H. G. Fletcher, Jr., and H. W. Diehl, Am. Soc. 74, 5774 (1952).

Aspergillus oryzae enzyme ←

Cleavage of glycosides ROR → ROH

s. 8, 14; s. a. B. 85, 1042, 1103 (1952)

Acetic anhydride/hydriodic acid *$(CH_3CO)_2O/HI$*

s. Hydriodic acid/acetic anhydride

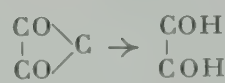
Carboxylic acids and mercaptans ←

Acidolysis ←

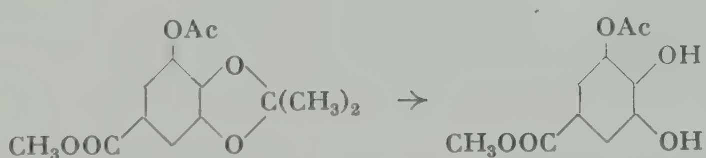
20. 

A mixture of 2-ethoxybenzothiazole (prepn. s. 834) and benzoic acid heated 24 hrs. at 170° with vigorous stirring in a dry N_2-atmosphere → 2-hydroxybenzothiazole (Y: 85%) and ethyl benzoate (Y: 77%). F. e. s., also thioethers with mercaptans, s. H. Gilman, K. E. Lentz, and J. A. Beel, Am. Soc. 74, 1081 (1952).

Acetic acid *CH_3COOH*

Cleavage of acetals 

s. 9, 303

21. 

Selective hydrolysis. A mixture of 3-acetyl-4.5-isopropylidenedihydroshikimate, acetic acid, methanol, and water refluxed 3 hrs., concentrated in vacuo, and the acetic acid removed by concentrating in vacuo three times after addition of alcohol → methyl 3-acetyldihydroshikimate.

Y: 82%. F. e. s. K. Freudenberg and J. Geiger, A. *575*, 145 (1952); s. a. R. Grewe and E. Nolte, A. *575*, 1 (1952); carbohydrate derivatives s. S. B. Baker, Am. Soc. *74*, 827 (1952).

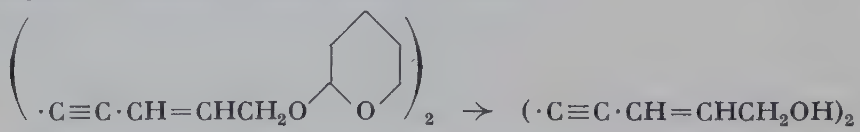
Hypophosphorous acid/hydrobromic acid *H_3PO_2/HBr*

s. Hydrobromic acid/hypophosphorous acid

p-Toluenesulfonic acid *TsOH*

Removal of protective groups ROR → ROH
Cleavage of tetrahydro-2-pyranyl ethers

22.

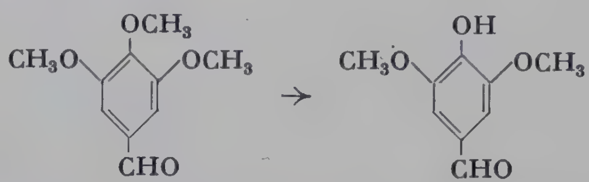


A soln. of 1,10-bis(tetrahydro-2′-pyranyloxy)deca-2,8-diene-4,6-diyne and a small amount of p-toluenesulfonic acid in alcohol refluxed 1 hr. → deca-2,8-diene-4,6-diyne-1,10-diol. Y: almost 100%. F. e. s. R. Ahmad and B. C. L. Weedon, Soc. *1953*, 3286.

Sulfuric acid *H_2SO_4*

Partial cleavage of methyl ethers

23.

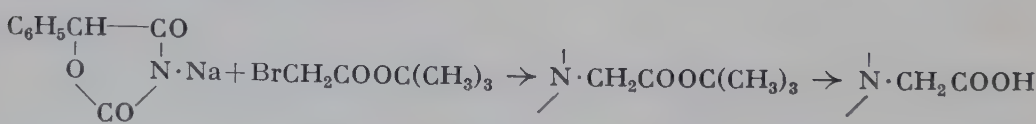


A mixture of 3,4,5-trimethoxybenzaldehyde and concd. H_2SO_4 kept 8 hrs. at 40°, then allowed to stand at room temp. overnight → syringaldehyde. Y: 96%. I. A. Pearl and D. L. Beyer, Am. Soc. *74*, 4262 (1952); s. a. K. Aghoramurthy and T. R. Seshadri, Soc. *1954*, 3065.

Aldehydes from 1,1-diacoxy compounds $CH(OAc)_2 \rightarrow CHO$
s. *9*, 251

N-Alkylation of oxazolidiones
Blocking of carboxyl groups
by formation of tert-butyl esters
Hydrolysis of carboxylic acid esters COOR → COOH
under anhydrous conditions

24.



Tert-butyl bromoacetate added with swirling during 15 min. to a soln. of the Na-salt of 5-phenyl-2,4-oxazolidione in dimethylformamide, al-

lowed to stand overnight, the resulting crude 3-carbo-*tert*-butoxymethyl-5-phenyl-2,4-oxazolidione dissolved in concd. H_2SO_4, then cooled and dil. with water → 3-carboxymethyl-5-phenyl-2,4-oxazolidione. Y: 87.3%.—*Tert*-butyl esters, which can be cleaved under anhydrous conditions, may be used to block carboxyl groups in sensitive compounds. Also hydrolysis with HCl-gas in dioxane s. J. C. Sheehan and G. D. Laubach, Am. Soc. *73*, 4752 (1951).

Hydrochloric acid *HCl*

Alcohols from alkoxymethyl ethers ROR → ROH
s. *9*, 270

Cleavage of acetals $\begin{matrix} CO \\ | \\ CO \end{matrix} \!\!>\! C \rightarrow \begin{matrix} COH \\ | \\ COH \end{matrix}$
s. *9*, 318

Cleavage of benzylidene derivatives of carbohydrates
s. *9*, 355

Oxo compounds from acetals $C(OR)_2 \rightarrow CO$
s. *9*, 665, 743, 903

Deacetylation OAc → OH
s. *7*, 27; partial deacetylation s. E. P. Oliveto et al., Am. Soc. *75*, 5486 (1953); A. Lardon and T. Reichstein, Pharm. Acta Helv. *27*, 287 (1952); large batches s. H. H. Inhoffen, H. Jahnke, and P. Nehring, B. *87*, 1154 (1954)

Ethylenecarboxylic acids from hydroxycarboxylic acid esters COOR → COOH

25. $C_6H_5CH(OH)CH_2COOC(CH_3)_3 \rightarrow C_6H_5CH{=}CHCOOH$

t-Butyl *β*-hydroxy-*β*-phenylpropionate refluxed 1.5 hrs. in concd. HCl-dioxane → cinnamic acid. Y: 96%. F. e. s. C. R. Hauser and W. H. Puterbaugh, Am. Soc. *75*, 1068 (1953).

Carboxylic acids from carboxylic acid esters
Selective hydrolysis
N-Thiocarbonylaminocarboxylic acids

26. $C_6H_5SCONHCH_2COOC_2H_5 \rightarrow C_6H_5SCONHCH_2COOH$

A suspension of phenylthiocarbonylglycine ethyl ester in a 1:1 mixture of glacial acetic acid and concd. HCl refluxed 10 min. → phenylthiocarbonylglycine. Y: 89%. F. e. s. A. Lindenmann, N. H. Khan, and K. Hofmann, Am. Soc. *74*, 476 (1952).

Carboxylic acids from carboxylic acid esters
Acidolysis

at room temp. s. *6*, 25; at reflux temp. s. K. Schlögl, F. Wessely, and G. Korger, M. *83*, 493 (1952)

Dicarboxylic acid monoesters
from dicarboxylic acid diesters
Acidolysis

27.

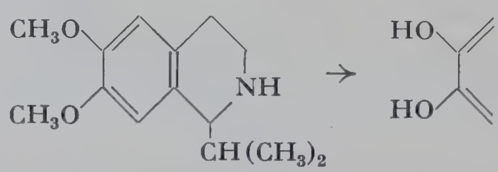
$$CH_3OOC \cdot CH_2C(CH_3)_2CH_2CH_2C(CH_3)_2CH_2 \cdot COOCH_3$$
$$\downarrow$$
$$CH_3OOC \cdot CH_2C(CH_3)_2CH_2CH_2C(CH_3)_2CH_2COOH$$

Dimethyl β,β,β'.β'-tetramethylsuberate refluxed with concd. HCl and an equimolecular quantity of acetic acid, methyl acetate removed as formed through a short column until 0.33 equivalent has distilled, further reaction stopped by adding benzene, the water removed by azeotropic distillation, and the procedure repeated several times with a mixture of tetramethylsuberic acid, obtained as by-product, and unchanged dimethyl ester → methyl hydrogen β,β,β',β'-tetramethylsuberate. Y: 83%. S. F. Birch et al., Soc. *1952*, 1363.

Hydrobromic acid/hypophosphorous acid *HBr/H_3PO_2*

Cleavage of methyl ethers ROR → ROH

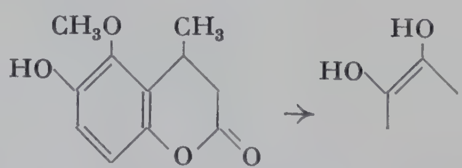
28.



1-Isopropyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (prepn. s. 84) heated with 10% excess 48%-HBr containing a little hypophosphorous acid, whereby the temp. reaches 126° after removal of the aq. forerun, and the product isolated after 1-3 hrs. when the evolution of methyl bromide ceases → 1-isopropyl-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline. Y: 90°. F. e. s. P. N. Craig et al., Am. Soc. *74*, 1316 (1952).

Hydriodic acid/acetic anhydride *$HI/(CH_3CO)_2O$*

29.



HI (d. 1.7) added to a soln. of 0.5 g. 5-methoxy-6-hydroxy-4-methylcoumarin (prepn. s. 199) in acetic anhydride, and refluxed 2 hrs. in an oil bath at 130-140°, then poured into $NaHSO_3$-soln. → 0.4 g. 5,6-dihydroxy-4-methylcoumarin. V. J. Dalvi, R. B. Desai, and S. Sethna, J. Indian Chem. Soc. *28*, 366 (1951).

Palladium *Pd*

Hydrogenolysis
of benzyl ethers ROR → ROH
s. *9*, 303

Palladium-carbon *Pd-C*

of benzyl esters COOR → COOH
s. *9*, 118, 434

of trityl ethers
s. *1*, 216; s. a. R. *72*, 365 (1953)

Simultaneous cleavage
of carbobenzoxy derivatives of amines
and benzyl esters
s. *9*, 860

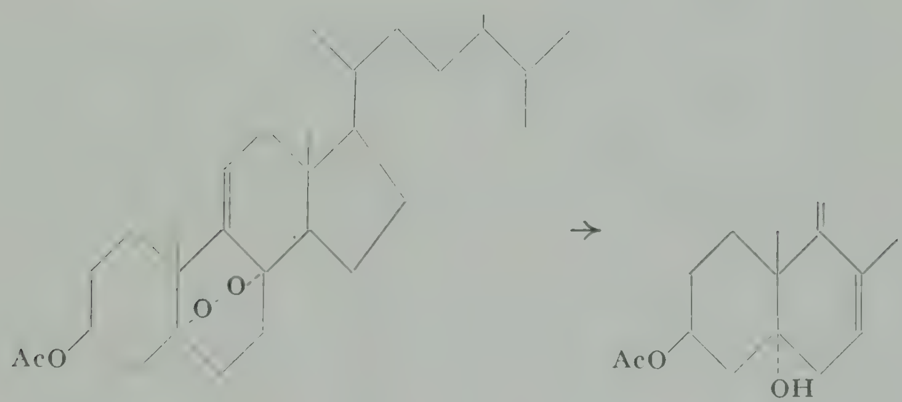
Elimination

Oxygen ↑ HO ⇑ O

Zinc/acetic acid *Zn/CH_3COOH*

Ethylenealcohols from peroxides C

30.



Zn-dust added in small portions to a boiling soln. of 20 g. 3β-acetoxy-5α,8α-epidioxyergost-9-ene in acetic acid, then refluxed 15 min. → 15 g. 3β-acetoxy-5α-hydroxyergosta-7,9-diene. F. e. s. P. Bladon et al., Soc. *1952*, 4883, 4890; *1953*, 2916, 2921.

Formation of H—N Bond

Uptake

Addition to Nitrogen HN ⇓ NN

Without additional reagents *w.a.r.*

Sulfonylhydrazomium salts from aminesulfonimides ←

s. *9*, 984

Electrolysis ↯

Hydrazines from diazonium salts $N_2^+ \rightarrow NHNH_2$

31. $$C_6H_5N{\equiv}N]^+Cl^- \rightarrow C_6H_5NHNH_2,HCl$$

Flow electrolysis. Phenyldiazonium chloride in 0.233 *M* HCl as catholyte passed during 2 hrs. at —15° through a flow electrolysis apparatus (s. original) with Pt-anode, Hg-cathode, 6.0 *N* H_2SO_4 as anolyte, using a current of 1.0 amp. → phenylhydrazine hydrochloride. Y: almost 100%.—By this procedure, an almost complete separation of startg. m. and end product is attained and the side reaction between them avoided. P. Rüetschi and G. Trümpler, Helv. *36*, 1649 (1953).

Phenylhydrazine $C_6H_5NHNH_2$

Hydrazo from azo compounds N:N → NHNH

s. *9*, 41

Hydrogen sulfide H_2S

Nitrohydrazo compounds

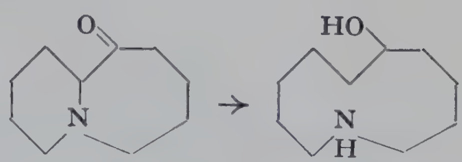
s. *1*, 19; (N-nitro)hydrazo compounds s. R. A. Henry, S. Skolnik, and G. B. L. Smith, Am. Soc. *75*, 955 (1953)

Addition to Nitrogen and Carbon HN ⇓ NC

Electrolysis ↯

Medium-N-heterocyclic alcohols from N-bicyclic ketones ⊂

32.



6-Keto-1-azabicyclo[5.4.0]hendecane electrolyzed at 60° with a Pb-cathode and 30%-H_2SO_4 as catholyte → 6-hydroxyazacyclohendecane.

Y: 71%. F. e. s. N. J. Leonard, S. Swann, Jr., and E. H. Mottus, Am. Soc. *74*, 6251 (1952).

Phosphorus/hydriodic acid *P/HI*

α-Aminocarboxylic acids from oxazolones
Reductive oxazolone ring opening

s. *5*, 17; s. a. J. P. Lambooy, Am. Soc. *76*, 133 (1954)

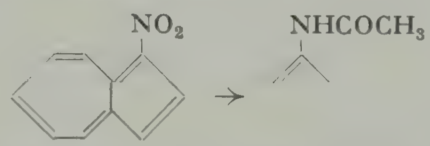
Exchange

Oxygen ↑ HN ⇅ O

Zinc *Zn*

Acylamines from nitro compounds $NO_2 \rightarrow NH$

33.



Zn-dust added during 5 min. to a stirred soln. of 1-nitroazulene and Na-acetate in acetic acid-acetic anhydride, and stirred 1 hr. → N-acetyl-1-azulylamine. Y: 90%. F. e. s. A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, Am. Soc. *75*, 4980 (1953).

Lithium aluminum hydride *$LiAlH_4$*

Unsym. hydrazines and amines from N-nitrosamines ←

34.

$$(CH_3)_2N\cdot NO \rightarrow (CH_3)_2N\cdot NH_2 \qquad (C_6H_5)_2N\cdot NO \rightarrow (C_6H_5)_2NH$$

$LiAlH_4$ in dry ether allowed to react over a period of 1 hr. with nitrosodimethylamine → unsym. dimethylhydrazine. Y: 78% | nitrosodiphenylamine → diphenylamine. Y: 74%.
F. W. Schueler and C. Hanna, Am. Soc. *73*, 4996 (1951); *74*, 3693 (1952).

Stannous chloride *$SnCl_2$*

Partial reduction of dinitro compounds $NO_2 \rightarrow NH_2$

s. *1*, 24/5; s. a. L. Sihlbom, Acta Chem. Scand. *6*, 1528 (1952)

Hydrazine/potassium hydroxide *$H_2N\cdot NH_2/KOH$*

Amines from nitro compounds with simultaneous reduction of oxo to hydrocarbon groups

s. *9*, 123

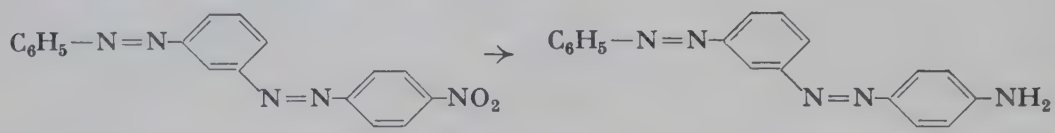
Hydrazine/nickel *$H_2N \cdot NH_2/Ni$*
s. Nickel/hydrazine

Sodium sulfide/sulfur *Na_2S/S*

s. *3*, 16; s. a. G. R. Ramage and G. Trappe, Soc. *1952*, 4406

Sodium hydrogen sulfide *NaHS*

Aminoazo from nitroazo compounds

35. 

Aq. NaHS added gradually during 30 min. to a boiling suspension of 3-(p-nitrophenylazo)azobenzene in ethanol, and refluxed for an additional hr. → 3-(p-aminophenylazo)azobenzene. Crude Y: 79.0%. F. e. s. K. Ueno, Am. Soc. *74*, 4508 (1952); s. a. C. M. Atkinson et al., Soc. *1954*, 2023.

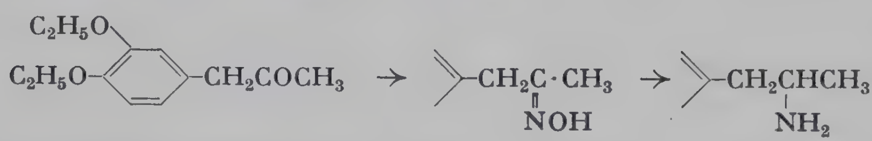
Hydrosulfite *$S_2O_4^{--}$*

Amines from nitro compounds $NO_2 \rightarrow NH_2$

s. *1*, 26; *4*, 25; pyrimidines s. B. R. Baker, J. P. Joseph, and R. E. Schaub, J. Org. Chem. *19*, 631 (1954)

Nickel *Ni*

Prim. amines from ketones via oximes $CO \rightarrow C{:}NOH \rightarrow CHNH_2$

36. 

Aq. Na-carbonate added during 15 min. to a stirred mixture of 1-(3′,4′-diethoxyphenyl)-2-propanone, water, and hydroxylamine hydrochloride, and stirring continued for an additional 2.5 hrs. → 1-(3′,4′-diethoxyphenyl)-2-propanone oxime (Y: 92%) mixed with abs. alcohol, liq. NH_3, and Raney-Ni, then heated under 200 atm. of H_2 with agitation whereupon reduction takes place between 80 and 120° during 1 hr. → 1-(3′,4′-diethoxyphenyl)isopropylamine (Y:88%). F. e. s. E. R. Shepard et al., Am. Soc. *74*, 4611 (1952).

5-Amino- from 5-nitrosopyrimidines $NO \rightarrow NH_2$

s. *9*, 448

Amines from nitro compounds $NO_2 \rightarrow NH_2$

Aliphatic compounds

s. *7*, 39; s. a. Org. Synth. *34*, 19 (1954); D. J. Cook, O. R. Pierce, and E. T. McBee, Am. Soc. *76*, 83 (1954); C. A. Grob and E. G. Jenny, Helv. *35*, 2106 (1952)

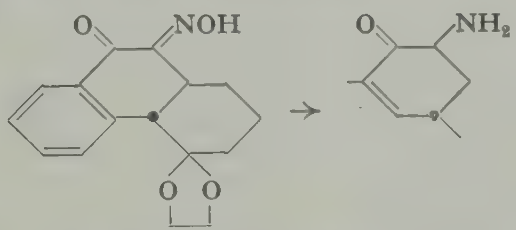
Nickel/hydrazine *$Ni/H_2N{\cdot}NH_2$*

37. With the addition of a small amount of Raney-Ni, hydrazine hydrate will selectively reduce an ar. nitro compound to an amine at room or steam-bath temp. To eliminate loss due to foaming a large excess of solvent alcohol is necessary.—E: 2-3 molar ratios of 100%-hydrazine hydrate added to p-nitrobiphenyl ether, placed on a steam bath, when just warm a small amount of Raney-Ni added, when the color has almost disappeared more catalyst added to decompose the excess hydrazine, and the soln. heated to boiling to drive off the dissolved gases → p-aminobiphenyl ether. Y: 96.5%.—Similarly: p-Aminocinnamic acid, m-aminobenzophenone. Y: 80-99%. F. e. s. D. Balcom and A. Furst, Am. Soc. *75*, 4334 (1953); s. a. D. S. Tarbell, R. F. Smith, and V. Boekelheide, Am. Soc. *76*, 2470 (1954).

Palladium-carbon *Pd-C*

α-Aminoketones from α-isonitrosoketones C:NOH → $CHNH_2$

38.



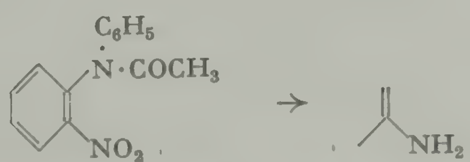
A suspension of 6 g. *trans*-1,2,3,4,9,10,11,12-octahydro-4,9-diketo-10-oximinophenanthrene 4-ethylene glycol ketal in alcohol hydrogenated 10 hrs. in the presence of 10%-Pd-charcoal at an initial pressure of 60 lbs./sq. in. → 5.4 g. 10-amino-1,2,3,4,9,10,11,12-octahydro-4,9-diketophenanthrene 4-ethylene glycol ketal. D. Ginsburg and R. Pappo, Soc. *1953*, 1524.

α-Aminoalcohols from α-isonitrosoketones COC:NOH
Stereospecific hydrogenation → $CH(OH)CHNH_2$
s. *9*, 74

Amines from nitro compounds $NO_2 \rightarrow NH_2$
s. *9*, 569

Platinum oxide *PtO_2*

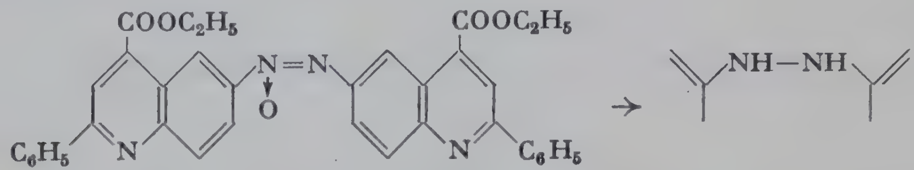
39.



o-Nitro-N-acetyldiphenylamine dissolved in the minimum volume of warm, aq. 50%-ethanol, and hydrogenated with PtO_2 at 40 p. s. i. →

o-amino-N-acetyldiphenylamine. Y: 76%.—2-Methyl-1-phenylbenzimidazole was obtained in 95%-ethanol. P. A. S. Smith et al., Am. Soc. *75*, 6335 (1953).

Hydrazo from azoxy compounds $\underset{\downarrow}{N{:}N}\rightarrow NHNH$ (O on N)

40. 

A mixture of 1 g. diethyl 2,2′-diphenyl-6,6′-azoxycinchoninate and pre-reduced PtO_2 in ethyleneglycol monomethyl ether hydrogenated 30 min. at an initial temp. of ca. 40° → 0.96 g. diethyl 2,2′-diphenyl-6,6′-hydrazocinchoninate. C. M. McCloskey, Am. Soc. *74*, 5922 (1952).

Nitrogen ↑ HN⇅N

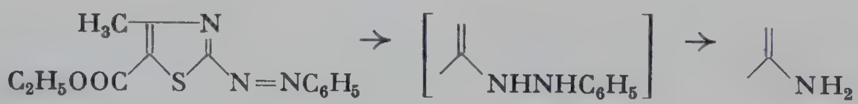
Lithium aluminum hydride *$LiAlH_4$*

Amines from N-nitrosamines N·NO → NH

s. *9*, 34

Phenylhydrazine *$C_6H_5NHNH_2$*

Amines from azo compounds via hydrazo compounds ←

41. 

Ethyl 2-phenylazo-4-methyl-5-thiazolecarboxylate heated with phenylhydrazine to 170°, and refluxed 5 min. at this temp. → ethyl 2-phenylhydrazo-4-methyl-5-thiazolecarboxylate (Y: 90%) heated with more phenylhydrazine at 200° → ethyl 2-amino-4-methyl-5-thiazolecarboxylate. Over-all Y: 72%. F. e., without isolation of the intermediate, and limitations, s. H. Beyer and G. Wolter, B. *85*, 1077 (1952).

Sulfur ↑ HN⇅S

Sodium *Na*

Cleavage of sulfonic acid amides $N{\cdot}SO_2R \rightarrow NH$

s. *3*, 21; in n-butanol s. H. Stetter, B. *86*, 197 (1953)

Sodium/liq. ammonia *Na/NH_3*

N-Detosylation N·Ts → NH

42. 24 g. tosyl-L-glutamine (prepn. s. 402) dissolved in liq. NH_3, Na added at the boiling point to give a permanent blue color, then *Dowex-50* resin in the NH_4-form added, whereby the color is discharged instantly, NH_3 evaporated, the flask thoroughly evacuated, water added, and the resin filtered off → 9 g. L-glutamine. A second new isolation technique whereby glacial acetic acid is added to the well-cooled liq. NH_3-soln. and f. e. s. J. M. Swan and V. du Vigneaud. Am. Soc. *76*, 3110 (1954).

Phenol/hydrobromic acid *C_6H_5OH/HBr*

s. Hydrobromic acid/phenol

Hydrochloric acid *HCl*

s. *3*, 22; s. a. A. Müller et al., M. *83*, 386 (1952)

Hydrobromic acid/phenol *HBr/C_6H_5OH*

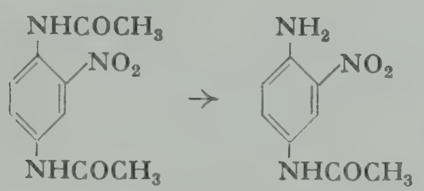
s. *8*, 29; s. a. D. I. Weisblat et al., Am. Soc. *75*, 5893 (1953)

Carbon ↑ HN⇅C

Sodium hydroxide *NaOH*

Partial N-deacylation NAc → NH

43.



Nitro-2,5-diacetamidobenzene stirred at 85° into aq. 5%-NaOH, and kept 50 min. at 85-90° → 4-acetamido-2-nitroaniline. Crude Y: 78-85%; pure Y: 60-64%. J. B. Polya, J. Applied Chem. *1*, 473 (1951).

Selective hydrolysis
Blocking of amino groups

44. 2 *N* NaOH added to a soln. of β-O-(2,3,4,6-tetraacetyl-D-glucosido)-N-trifluoroacetyl-3,5-diiodo-L-thyronine methyl ester in ethanol-acetone, and stirred 5 hrs. → β-O-D-glucosido-3,5-diiodo-L-thyronine. Y: 91%.— Trifluoroacetyl is an excellent amino blocking group for the preparation of free glucosides and glucuronosides because it is readily removed by treatment with dil. alkali at room temp., a procedure which does not affect the glucoside or glucuronoside linkage. F. e. s. A. Taurog, S. Abraham, and I. L. Chaikoff. Am. Soc. *75*, 3473 (1953).

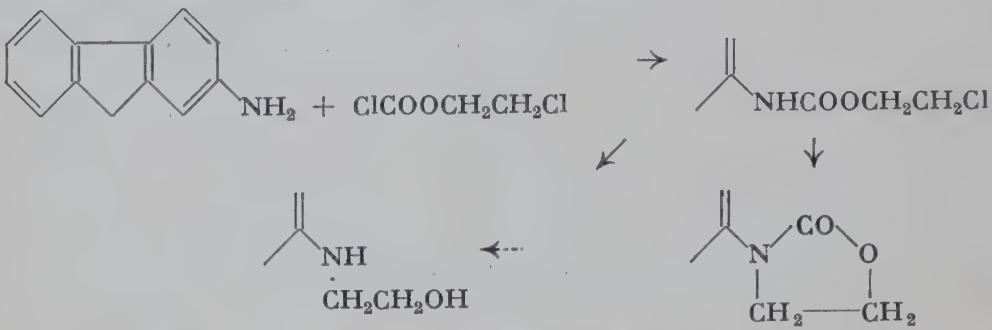
Potassium hydroxide *KOH*

Amines from acylamines NAc → NH

in ethylene glycol s. *8*, 195; s. a. W. M. Lauer and R. G. Lockwood, Am. Soc. *76*, 3974 (1954)

2-Aminoalcohols and 2-oxazolidones from amines via halogenourethans ←

45.



β-Chloroethyl chlorocarbonate added dropwise to an ice-cold stirred soln. of 2-aminofluorene in pyridine, and stirring continued for 0.5 hr. at 0-10° → β-chloroethyl N-2-fluorenylcarbamate (Y: 95%), 2.88 g. in hot alcohol treated with a soln. of

1.6 g. KOH in ethanol, stirred until a precipitate is formed, cooled to room temp., and stirring continued for 0.5 hr. → 3-(2′-fluorenyl)-2-oxazolidone (Y: 95%).	3.2 g. KOH in ethanol, and vigorously refluxed for 2 hrs. → 2-β-hydroxyethylaminofluorene (Y: 89%).

E. Sawicki, Am. Soc. *75*, 4596 (1953).

Sodium/liq. ammonia *Na/NH₃*

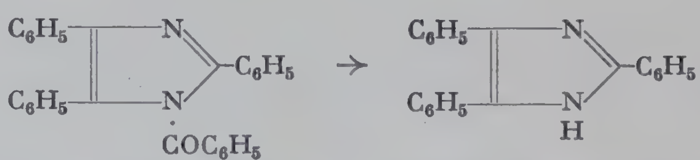
N-Decarbobenzoxylation with simultaneous formation of mercaptans from benzylthioethers NCOOR → NH

s. *9*, 56

Ammonium acetate *CH_3COONH_4*

N-Deacylation NAc → NH

46.



A mixture of N-benzoyllophine, NH_4-acetate, and acetic acid refluxed 1 min. → lophine. Y: ca. 100%.—In acetic acid alone a reflux time of 15 min. is necessary. M. Weiss, Am. Soc. *74*, 5193 (1952).

Hog kidney enzyme ←

Resolution of racemates by enzymic hydrolysis
Amines from acylamines

s. *6*, 42; s. a. J. P. Greenstein et al., Biochem. Prep. *3*, 84 (1953); J. Biol. Chem. *203*, 333 (1953)

Phosphonium iodide *PH_4I*

Amines from urethans NCOOR → NH
Cleavage of carbobenzoxy derivatives of amines

s. *2*, 138; *3*, 25; cf. N. F. Albertson and F. C. McKay, Am. Soc. *75*, 5323 (1953)

Phosphoric acid *H_3PO_4*

Amines from acylamines NAc → NH

s. *2*, 51; s. a. W. Bradley and J. V. Butcher, Soc. *1954*, 2311

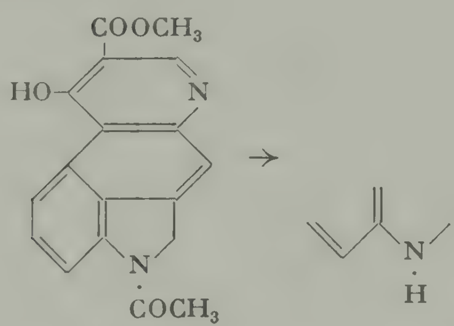
Sulfuric acid *H_2SO_4*

s. *9*, 416; s. a. C. M. Atkinson et al., Soc. *1954*, 2023

Sulfuric acid/ammonium chloride *H_2SO_4/NH_4Cl*

Selective N-deacylation

47.



A mixture of 5 g. 4-acetyl-4,5-dihydro-9-carbethoxy-10-hydroxyindolo-[4,3-f.g]quinoline, NH_4Cl, alcohol, H_2SO_4, and water heated 35 min. at 100° in a sealed tube with occasional shaking → 3.5 g. 4,5-dihydro-9-carbethoxy-10-hydroxyindolo[4,3-f,g]quinoline. A. Stoll and T. Petrzilka, Helv. *36*, 1137 (1953).

Hydrochloric acid *HCl*

Aminosulfonic acid amides from acylaminosulfonic acid amides

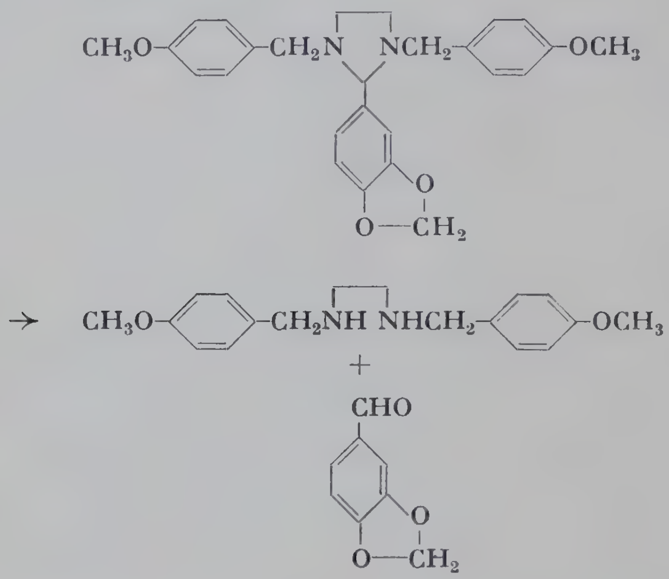
s. *9*, 392

Aminoalcohols from halogenoacylamines
s. *9*, 330

Imidazoles from isoimidazoles with hydrolysis ←
s. *9*, 420

Imidazolidine ring opening C

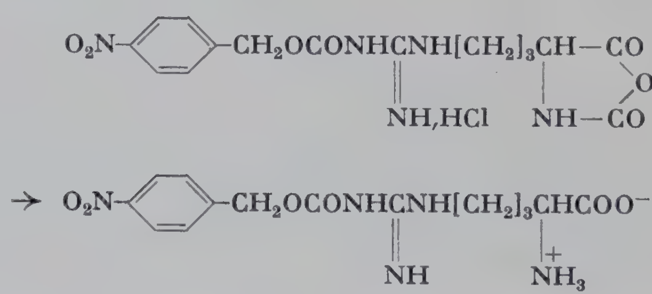
48.



1,3-Bis-(p-methoxybenzyl)-2-(3′,4′-methylenedioxyphenyl)tetrahydroimidazole shaken ca. 10 min. with 10%-HCl followed by extraction with ether → piperonal and 1,2-bis-(p-methoxybenzylamino)ethane dihydrochloride. Y of both: ca. 100%. J. H. Billman, J. Y. Chen Ho, and L. R. Caswell, J. Org. Chem. *17*, 1375 (1952).

***α*-Aminocarboxylic acids from 2,5-oxazolidiones**

49.



A soln. of N^{ω}-p-nitrobenzyloxycarbonyl-L-arginine-N-carboxylic acid anhydride hydrochloride in dimethylformamide added at 30° during 80 min. with stirring to 0.5 *N* HCl, and stirring continued for 30 min. → N^{ω}-p-nitrobenzyloxycarbonyl-L-arginine. Y: 83%. D.T.Gish and F.H. Carpenter, Am. Soc. *75*, 5872 (1953).

Hydrobromic acid *HBr*

Amines from urethans NCOOR → NH

50. $\begin{array}{l} CH_2CONHCH_2COOH \\ | \\ NHCOOCH_2C_6H_5 \end{array} \rightarrow \begin{array}{l} CH_2CONHCH_2COOH \\ | \\ NH_2 \end{array}$

A stream of HBr bubbled into a suspension of carbobenzoxyglycylglycine in warm *nitromethane* for 5 min., then allowed to stand for 3 hrs. → glycylglycine. Y: 81-90%.—Because of the speed and simplicity of this method it should be useful in many cases of peptide synthesis, particularly with compounds containing reducible groups. F. e. s. N. F. Albertson and F. C. McKay, Am. Soc. *75*, 5323 (1953).

51. $\begin{array}{l} \qquad\qquad CH_2C_6H_5 \\ CH_2CONHCHCOOCH_2C_6H_5 \\ | \\ NHCOOCH_2C_6H_5 \end{array} \rightarrow \begin{array}{l} \qquad\qquad CH_2C_6H_5 \\ CH_2CONHCHCOOCH_2C_6H_5 \\ | \\ NH_2,HBr \end{array}$

Selective elimination of N-carbobenzoxy groups. A 33% soln. of HBr in glacial acetic acid added to carbobenzoxyglycyl-L-phenylalanine benzyl ester, and allowed to stand at room temp. with occasional shaking until CO_2-evolution ceases → glycyl-L-phenylalanine benzyl ester hydrobromide. Y: 89%. F. e. s. D. Ben-Ishai, J. Org. Chem. *19*, 62 (1954).

Palladium *Pd*

N-Decarbobenzoxylation of amines and carboxylic acid hydrazides

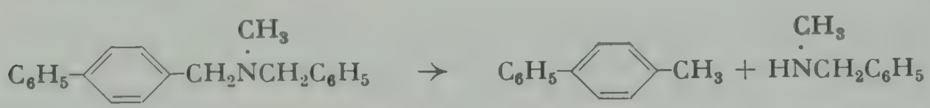
52. $$C_6H_5CH_2OOC\cdot NHCH_2CONHCH_2CONHCH_2CONHNHCOOCH_2C_6H_5$$
$$\downarrow$$
$$H_2NCH_2CONHCH_2CONHCH_2CONHNH_2$$

A suspension of carbobenzoxytriglycine carbobenzoxyhydrazide in aq. 50%-methanol and 3 *N* HCl hydrogenated with spongy Pd until the evolution of CO_2 ceases → triglycine hydrazide dihydrochloride. Y: 91%. K. Hofmann et al., Am. Soc. *74*, 470 (1952).

Palladium-carbon *Pd-C*

Hydrogenolysis of amines NR → NH

53.



N-Methyl-N-benzyl-p-phenylbenzylamine in alcohol hydrogenated 2.5 hrs. with Pd-C at room temp. and atmospheric pressure → p-phenyltoluene (Y: 89%) and N-methylbenzylamine (Y: 70% as the hydrochloride) (*35*, 1348).—Raney-Ni and PtO_2 tend to ring hydrogenation. Instead of the free bases their salts can be used (*35*, 1162). The ease of

splitting increases in the following order: methyl < benzyl < p-phenylbenzyl < benzhydryl, 9-fluorenyl, 1- and 2-methylnaphthyl (*35*, 1348). F. e. s. H. Dahn, U. Solms, and P. Zoller, Helv. *35*, 1162, 1348, 2117 (1952); s. a. R. Baltzly and P. B. Russell, Am. Soc. *75*, 5598 (1953).

Simultaneous cleavage of carbobenzoxy derivatives of amines and benzyl esters NCOOR → NH

s. *9*, 860; s. a. D. Ben-Ishai, J. Org. Chem. *19*, 62 (1954)

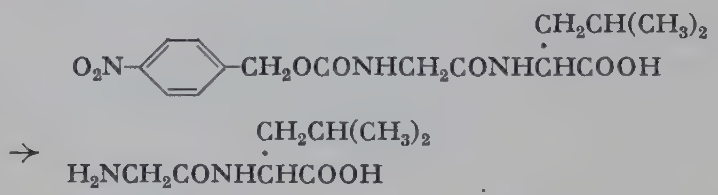
Palladous oxide *PdO*

N-Debenzylation $NCH_2C_6H_5 \rightarrow NH$

s. *1*, 37; s. a. W. G. Finnegan, R. A. Henry, and E. Lieber, J. Org. Chem. *18*, 779 (1953)

Cleavage of carbo-p-nitrobenzoxy derivatives of peptides NCOOR → NH

54.



H_2 bubbled through a soln. of carbo-p-nitrobenzyloxyglycyl-L-leucine in methanol in the presence of PdO and acetic acid → glycyl-L-leucine. Y: 97%. F. H. Carpenter and D. T. Gish, Am. Soc. *74*, 3818 (1952); *75*, 5872 (1953).

Formation of H—S Bond

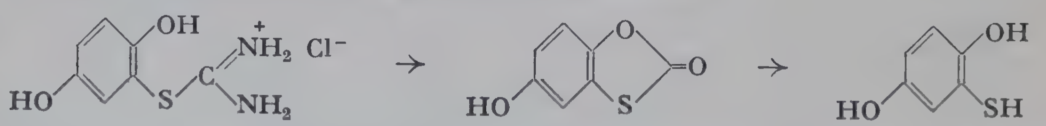
Exchange

Carbon ↑ **HS⇅C**

Sodium hydroxide *NaOH*

Benz-1,3-oxathiolone ring closure and opening ←

55.



A soln. of 2.2 g. S-2,5-dihydroxyphenylthiouronium chloride and Na-acetate in acetic acid-water refluxed 2 hrs. → 1.3 g. 5-hydroxy-1,3-benzoxathiol-2-one dissolved in O_2-free 2 *N* NaOH in a N_2-atmosphere.

boiled 1 hr. in a stream of O_2-free N_2, allowed to cool in N_2 to room temp., and acidified with 2 N H_2SO_4, whereupon evolution of some CO_2 occurs → mercaptoquinol (Y: almost 100%). H. Burton and S. B. David, Soc. *1952*, 2193.

Sodium/liq. ammonia *Na/NH_3*

Mercaptans from benzyl thioethers with simultaneous N-decarbobenzoxylation $RSCH_2C_6H_5 \rightarrow RSH$

56. $C_6H_5CH_2OCONHCH_2CH_2CONHCH_2CH_2SCH_2C_6H_5$

$\rightarrow H_2NCH_2CH_2CONHCH_2CH_2SH$

Na added in small pieces with occasional agitation to a suspension of 2-benzylthio-N-(carbobenzoxy-β-alanyl)ethylamine in liq. NH_3 until the blue color is permanent for 45 min., then excess Na destroyed by NH_4-chloride, and the product isolated as the hydrochloride → N-β-alanyl-2-mercaptoethylamine. Y: ca. 100%. J. Baddiley and E. M. Thain, Soc. *1952*, 800.

Formation of H—Rem Bond

Exchange

Halogen ↓ HRem⇅Hal

Sodium carbonate *Na_2CO_3*

Phosphines from chlorophosphines by disproportionation ←

57. $4(C_6H_5)_2PCl + 3Na_2CO_3 + H_2O \rightarrow 2(C_6H_5)_2PH + 2(C_6H_5)_2PO_2Na + 3CO_2 + 4NaCl$

Diphenylchlorophosphine (prepn. s. 727) added dropwise during 30 min. under N_2 to an agitated aq. soln. of Na-carbonate, then warmed to 50°, and stirred for a further 30 min. → diphenylphosphine (startg. m. f. 709). Y: 47%. F. G. Mann and I. T. Millar. Soc. *1952*, 4453.

Remaining Elements ↓ HRem⇅Rem

Sodium/liq. ammonia *Na/NH_3*

Selenols from diselenides $RSeSeR \rightarrow 2RSeH$

58. $CH_3SeSeCH_3 \rightarrow 2CH_3SeH$

Dimethyl diselenide and Na added alternately to boiling liq. NH_3, then the NH_3 allowed to boil away → methaneselenol. Y: almost 100%. G. E. Coates, Soc. *1953*, 2839.

Formation of H—C Bond

Uptake

Addition to Oxygen and Carbon HC ⇓ OC

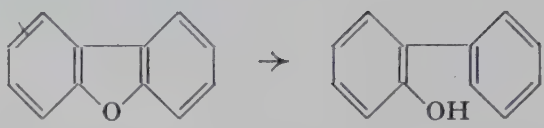
Irradiation/acetic acid ←

s. Acetic acid/irradiation

Lithium *Li*

Ring opening of heterocyclics

59.



Dibenzofuran, Li, and dry dioxane gently refluxed 12 hrs. with rapid stirring, filtered, cooled, and treated with water-dioxane → o-hydroxydiphenyl. Y: 77.2%. F. e. s. H. Gilman and D. L. Esmay, Am. Soc. 75, 2947 (1953).

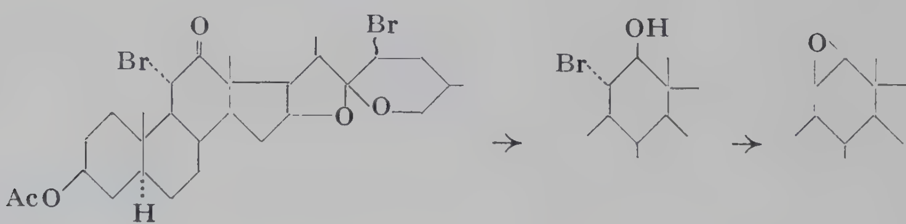
Lithium iodide/sodium boron hydride *$LiI/NaBH_4$*

s. Sodium boron hydride/lithium iodide

Lithium boron hydride *$LiBH_4$*

Oxido compounds from α-bromoketones via bromohydrins CO → CHOH

60.



A 2 *M* soln. of $LiBH_4$ in tetrahydrofuran added dropwise at 0° with stirring during 1.5 hrs. to a soln. of 11α,23ξ-dibromohecogenin acetate in tetrahydrofuran, and stirring continued for 10.5 hrs. at 0° → crude 3β-acetoxy-11α,23ξ-dibromo-12β-hydroxy-5α,22a-spirostane (Y: 80,6%) dissolved in anhydrous pyridine, shaken 48 hrs. with freshly precipitated dry Ag_2O in the dark, more Ag_2O added, shaking continued for

72 hrs., and the crude product reacetylated → 3β-acetoxy-11β,12β-oxido-23ξ-bromo-5α,22a-spirostane (Y from pure bromohydrin 90.2%). Over-all Y: 52.8%. J. Schmidlin and A. Wettstein, Helv. *36*, 1241 (1953).

Sodium boron hydride/lithium iodide *$NaBH_4/LiI$*

Diols from ketocarboxylic acid esters ←

s. *9*, 876

Sodium boron hydride *$NaBH_4$*

Alcohols from oxo compounds CO → CHOH

61. Slow reacting aldehyde and keto groups in cardioactive glycosides and aglycones can readily be reduced with $NaBH_4$. E. s. A. Hunger and T. Reichstein, B. *85*, 635 (1952).

62. $CH_3COCH_2CH_2CH_2NO_2 \rightarrow CH_3CH(OH)CH_2CH_2CH_2NO_2$

Nitroalcohols. An aq. soln. of $NaBH_4$ containing 1 drop concd. NaOH added dropwise at 20-25° during 1 hr. to a slowly stirred mixture of 5-nitro-2-pentanone and methanol, while the pH is kept at 3-4 by continuous addition of 3 *N* H_2SO_4, then allowed to stand for 5 min. → 5-nitro-2-pentanol. Y: 86.6%.—In general, use of $NaBH_4$ is to be preferred over Al-isopropoxide for reduction of sensitive compounds. F.e., also with Al-isopropoxide, s. H. Shechter, D. L. Ley, and L. Zeldin, Am. Soc. *74*, 3664 (1952).

63. $C_6H_5COCOOH \rightarrow C_6H_5CH(OH)COOH$

Special cases—Inverse addition method. Aq. phenylglyoxylic acid neutralized with dil. NaOH, added dropwise during 0.5 hr. at 10-18° to a vigorously stirred aq. soln. of $NaBH_4$, evaporated to dryness under reduced pressure, neutralized with concd. HCl-methanol, excess methanolic 4%-HCl added, the resulting *methyl borate removed* under reduced pressure until a portion of the soln., when ignited, burns with a pale blue flame, the remainder of the methanol evaporated, and the methyl mandelate hydrolyzed by refluxing 1 hr. with excess aq. 10%-NaOH → mandelic acid. Y: 76%. F.e., also with addition of $NaBH_4$ to the start. m., s. E. B. Reid and J. R. Siegel, Soc. *1954*, 520.

Lithium aluminum hydride *$LiAlH_4$*

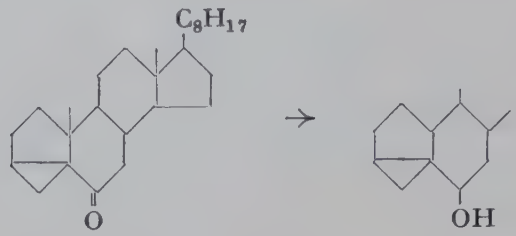
Sec. alcohols from ketones

s. *9*, 109, 352, 951

Stereoisomeric steroids

s. *6*, 55; 11-hydroxysteroids s. R. H. Levin et al., Am. Soc. *76*, 546 (1954)

64.



Stereochemistry of isosteroids. C_6-Epimers of 3,5-cyclo-stanols are solely formed from 3,5-cyclo-stanones with excess $LiAlH_4$.—E: 21.5 g. i-cholestan-6-one in ether → 18.5 g. epi-i-cholesterol. F. e. s. A. F. Wagner, N. E. Wolff, and E. S. Wallis, J. Org. Chem. *17*, 529 (1952).

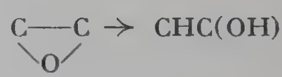
65.

A clear soln. of $LiAlH_4$ in anhydrous ether added dropwise with stirring to 2-acetylpyrrole in dry ether, and refluxing continued 30 min. on a steam bath → 2-pyrrolemethylcarbinol. Y: 80%.—Overreduction is avoided by *inverse addition* of $LiAlH_4$. F. e. s. W. Herz and C. F. Courtney, Am. Soc. *76*, 576 (1954).

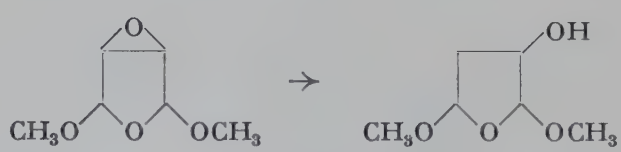
Sec. ethylenealcohols from ethyleneketones

s. *6*, 56; s. a. F. Bohlmann, B. *85*, 1144 (1952)

Alcohols from oxido compounds



66.

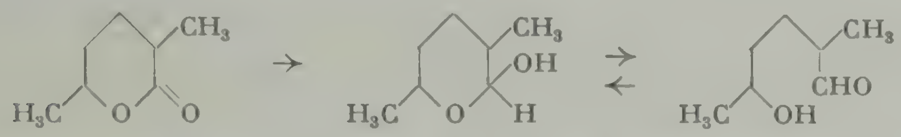


A soln. of 3,4-epoxy-2,5-dimethoxytetrahydrofuran in dry ether added dropwise during 40 min. to a suspension of $LiAlH_4$ in ether at a rate to maintain reflux temp., and stirring continued for 2 hrs. → 3-hydroxy-2,5-dimethoxytetrahydrofuran. Y: 87%. J. C. Sheehan and B. M. Bloom, Am. Soc. *74*, 3825 (1952).

Glycols from α-acoxyketones C(OAc)CO → C(OH)CH(OH)

s. *9*, 227

Hydroxyaldehydes from lactones C

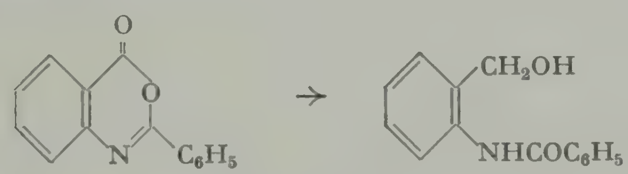
67. 

Slightly over ¼ mole of a 4% soln. of $LiAlH_4$ in tetrahydrofuran added slowly at –10 to –15° over a 20 min. period to a soln. of α-methyl-δ-caprolactone in tetrahydrofuran, and stirring continued for 1 hr. while the mixture is allowed to warm to room temp. → α-methyl-δ-hydroxycaproaldehyde. Y: 64.5%.—The yields varied between 64 and 84% in ether, tetrahydrofuran, or mixtures of both. F. e. s. G. E. Arth, Am. Soc. *75*, 2413 (1953); steric limitations s. M. Hinder and M. Stoll, Helv. *37*, 1866 (1954).

Partial reduction of lactams

s. *9*, 842

3,1-Benzoxazine ring opening

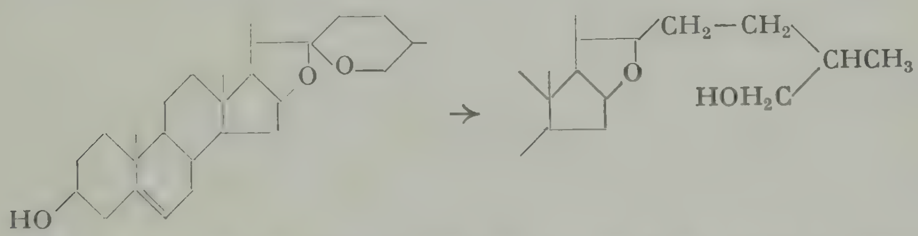
68. 

$LiAlH_4$ added to a suspension of 2-phenyl-3,1-benzoxaz-4-one in ether, and refluxed 1 hr. → o-benzoylaminobenzyl alcohol. Y: 84%. B. Witkop, J. B. Patrick, and H. M. Kissman, B. *85*, 949 (1952).

Lithium aluminum hydride/hydrochloric acid *$LiAlH_4/HCl$*

Partial reductive ring opening of O-heterocyclics ←

Furostane from spirostane ring

69. 

An ethereal soln. of diosgenin satd. at room temp. with anhydrous HCl. $LiAlH_4$ in pea-size amounts then added with vigorous stirring, sufficient time being allowed for each piece to react before the next piece is added, and gently refluxed for 2 hrs., excess HCl being maintained throughout the reaction → dihydrodiosgenin. Y: 90%. F. e., also with HBr. s. H. M. Doukas and T. D. Fontaine, Am. Soc. *75*, 5355 (1953).

Reductions with

Sodium trimethoxyboron hydride *$NaBH(OCH_3)_3$*

Alcohols from oxo compounds CO → CHOH

70. $C_6H_5CH{=}CHCHO \rightarrow C_6H_5CH{=}CHCH_2OHCH$

Sodium trimethoxyboron hydride readily reduces aldehyde, ketone, acid chloride, and acid anhydride groups. Ester and nitrile groups are only slowly reduced at elevated temp., whereas the carboxylate group does not appear to react. The nitro group is not reduced at lower temp., but undergoes reaction at 140°. Double bonds appear stable, even when conjugated with a carbonyl group. At low temp. sodium trimethoxyboron hydride in stoichiometric amounts appears to react with acid chlorides to form aldehydes.—E: Cinnamaldehyde added to a mixture of Na-trimethoxyboron hydride and ether, whereby refluxing sets in, which is continued for 4 hrs. by external heating → cinnamyl alcohol. Y: 79%. F. e. s. H. C. Brown and E. J. Mead, Am. Soc. *75*, 6263 (1953).

Aluminum alkoxide *$Al(OR)_3$*

Meerwein-Ponndorf-Verley reduction

Sec. alcohols from ketones CO → CHOH

s. *6*, 63, 65; *7*, 891; nitroalcohols s. *9*, 62; quinoline derivatives s. H. de Diesbach et al., Helv. *35*, 2322 (1952); effect of solvent s. E. D. Williams, K. A. Krieger, and A. R. Day, Am. Soc. *75*, 2404 (1953)

Yeast ←

Biochemical reduction
Partial reduction of steroid keto groups

reduction of 17-keto groups s. *8*, 51; of 3-keto-groups s. B. Camerino, C. G. Alberti, and A. Vercellone, Helv. *36*, 1945 (1953)

Acetic acid/irradiation ←

Sec. alcohols from ketones by photoreduction

s. *9*, 731

Phosphorus/iodine *P/I*

Carboxylic acids from phthalides

s. *9*, 366

Phosphorus/hydriodic acid *P/HI*

71.

from alkylidenephthalides. A mixture of benzalphthalide, HI, and red P refluxed 9-10 hrs. → dibenzyl-o-carboxylic acid. Y: 75-79%. T. W.

Campbell, R. Ginsig, and H. Schmid, Helv. *36*, 1489 (1953); carboxylic acids from phthalides in xylene s. E. Clar and D. G. Stewart, Soc. *1951*, 3215.

Nickel *Ni*

Prim. alcohols from aldehydes $CHO \rightarrow CH_2OH$

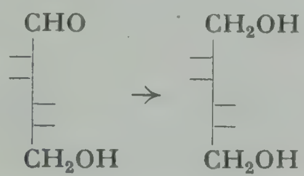
s. *6*, 68; s. a. R. I. Longley, Jr., and W. S. Emerson, Org. Synth. *34*, 71 (1954)

Sec. alcohols from ketones $CO \rightarrow CHOH$

s. *9*, 352

Polyalcohols from carbohydrates

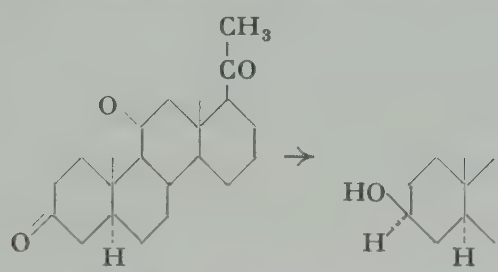
72.



D-Mannose refluxed 1.5 hrs. with Raney-Ni in aq. 70%-ethanol → D-mannitol. Y: 79%. F. e. s. J. V. Karabinos and A. T. Ballun, Am. Soc. *75*, 4501 (1953).

Partial reduction of steroid keto groups

73.



0.5 g. allopregnane-3,11,20-trione in ethanol hydrogenated 2 hrs. with prereduced Raney-Ni W 2 at room temp. and atmospheric pressure, whereupon slightly more than 1 mole of H_2 is consumed → 0.4 g. allopregnan-3β-ol-11.20-dione. F. e. s. C. Djerassi et al., Am. Soc. *75*, 3505 (1953).

Hydroxycarboxylic acid esters from ketocarboxylic acid esters

s. *7*, 75; s. a. M. Viscontini and H. Köhler, Helv. *37*, 41 (1954)

cis-trans-Isomers

s. *9*, 76

Palladium-carbon *Pd-C*

α-Aminoalcohols from α-isonitrosoketones COC:NOH
Stereospecific hydrogenation → $CH(OH)CHNH_2$

74. $$C_6H_5CO\underset{\overset{\|}{NOH}}{C}\cdot COOC_2H_5 \rightarrow C_6H_5\underset{OH}{CH}-\underset{NH_2}{CH}COOC_2H_5$$

A soln. of 22.1 g. ethyl benzoyloximinoacetate in 3 *N* abs. ethanolic HCl hydrogenated with Pd-on-Nuchar → 15.4 g. *erythro-β*-phenylserine ethyl ester. Yen-tsai Chang and W. H. Hartung, Am. Soc. *75*, 89 (1953).

Platinum oxide *PtO_2*

Glycols from acyloins COCH(OH) → CH(OH) CH(OH)

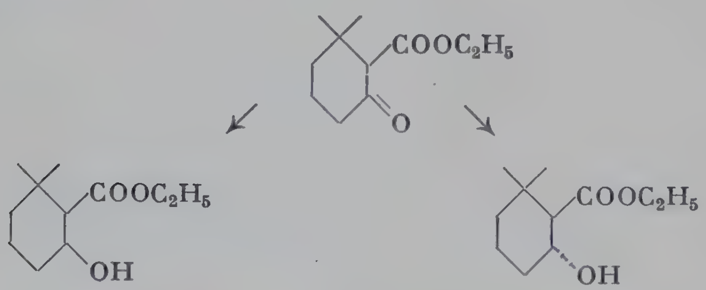
75. $$R\cdot COCH(OH)R \rightarrow R\cdot CH(OH)CH(OH)R$$
$$(CH_3)_3CHCH_2CH(CH_3)CH_2- \quad =R$$

6-Hydroxy-2,2,4,9,11,11-hexamethyldodecan-7-one in ethanol hydrogenated with PtO_2 at 20°/3-5 atm. → 2,2,4,9,11,11-hexamethyldodecane-6,7-diol. Y: 81%. E. E. and L. Turner, Soc. *1952*, 1761.

Platinum oxide/acetic acid *PtO_2/CH_3COOH*

Hydroxycarboxylic acid esters CO → CHOH
from ketocarboxylic acid esters
cis-trans-Isomers

76.



Ethyl 6,6-dimethyl-2-oxocyclohexanecarboxylate hydrogenated with

PtO_2 in acetic acid →	Raney-Ni in methanol →

ethyl 6,6-dimethyl-2-hydroxycyclohexanecarboxylate

3.85 g. *cis* from 3.96 g.	19.4 g. *trans* from 19.8 g.

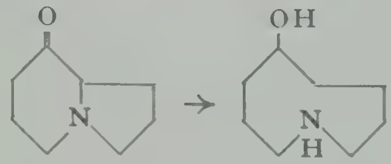
R. Helg and H. Schinz, Helv. *35*, 2406 (1952).

Addition to Nitrogen and Carbon HC ⇓ NC

Electrolysis

Reductive ring opening
Medium N-heterocyclics
from N-condensed rings

77.



8-Ketoöctahydropyrrocoline electrolyzed at ca. 60° with a Pb-cathode in 30%-H_2SO_4 at a current density of 0.05 amp./cm² until 4.5-5.0 F/mole have passed through → 5-hydroxyazacyclononane. Y: up to 73%. F. e. s. N. J. Leonard, S. Swann, Jr., et al., Am. Soc. *74*, 4620 (1952); *76*, 3193 (1954).

Sodium/liq. ammonia *Na/NH₃*

Thiosemicarbazides from thiosemicarbazones C:N → CHNH

78.

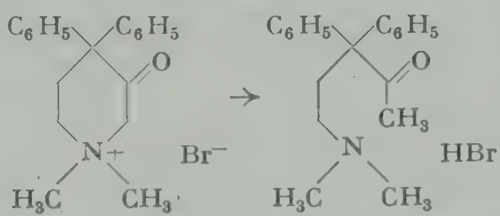
Small pieces of Na added to a suspension of 4-acetamidobenzaldehyde thiosemicarbazone in liq. NH_3, then NH_4Cl added to discharge the persistent blue color → 1-(4-acetamidobenzyl)-3-thiosemicarbazide. Y: 47%.—The use of Na/liq. NH_3 might be somewhat preferable to the Na-amalgam method (cf. Synth. Meth. *7*, 76; J. Bernstein et al., Am. Soc. *73*, 906 (1951)) because it is less likely to hydrolize alkali-labile groups. R. Duschinsky and H. Gainer, Am. Soc. *73*, 4464 (1951).

Zinc *Zn*

α-Aminocarboxylic acids from
α-ketocarboxylic acid hydrazones
in alcohol containing HCl s. *7*, 77; in acetic acid s. Ж. *23*, 847 (1953); C. A. *48*, 4443 h

Reductive piperidone ring opening

79.



Zn-dust added during 1 hr. to a warm mixture of 1-methyl-4,4-diphenyl-3-piperidone methobromide, heated on a steam bath until all of the Zn

has dissolved, and the product isolated as the hydrobromide → 3,3-diphenyl-5-dimethylamino-2-pentanone hydrobromide. Y: 79%. F. F. Blicke and J. Krapcho, Am. Soc. *74*, 4001 (1952).

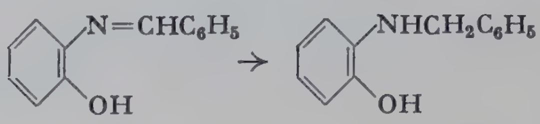
Lithium aluminum hydride *$LiAlH_4$*

Prim. amines from nitriles $CN \rightarrow CH_2NH_2$

s. *4*, 60; s. a. F. F. Blicke and Eu-Phang Tsao, Am. Soc. *75*, 5417 (1953)

Sec. amines from azomethines $C{:}NR \rightarrow CHNHR$

80.



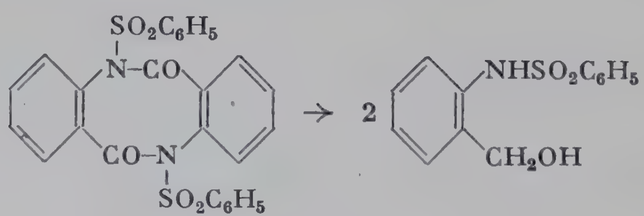
6.9 g. o-benzylideneaminophenol in dry ether added during 20 min. to a stirred suspension of $LiAlH_4$ in dry ether so that gentle refluxing takes place, then heated 1 hr. on a steam bath → 6.3 g. o-benzylaminophenol (startg. m. f. 509).—Other methods were not successful. F. e. s. B. Boothroyd and E. R. Clark, Soc. *1953*, 1499; s. a. J. Thesing, B. *87*, 507 (1954).

Selective ring hydrogenation of N-heterocyclics $C{:}N \rightarrow CHNH$

s. *6*, 75; s. a. F. Bohlmann, B. *85*, 390 (1952); K. W. Rosenmund, F. Zymalkowski, and N. Schwarte, B. *87*, 1229 (1954)

Reductive dianthranilide ring opening C

81.

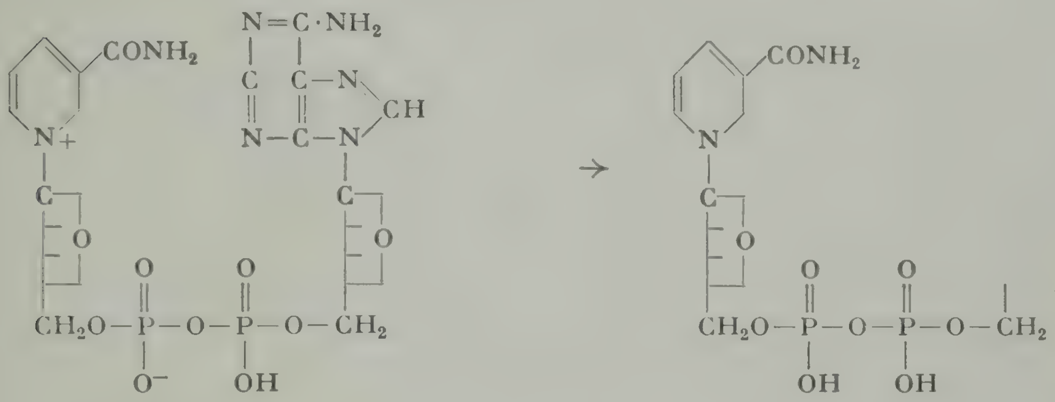


N,N'-Bis(benzenesulfonyl)dianthranilide in benzene added portionwise to $LiAlH_4$ in ether, refluxed 3 hrs., and allowed to stand overnight at room temp. → o-(phenylsulfonamido)benzyl alcohol. Y: 87%. F. e. s. A. Mustafa, Soc. *1952*, 2435.

Hydrosulfite *$S_2O_4^{--}$*

Aminophosphoric acids from inner quaternary ammonium phosphates ←

82.



Diphosphopyridine nucleotide (purity 86%) dissolved in 1.3% $NaHCO_3$, Na-hyposulfite quickly added with swirling, gassed with 95% N_2—5% CO_2, the vessel closed, kept 2 hrs. at 25°, then vigorously gassed with O_2 for 15 min. to oxidize excess hyposulfite, and isolated as the Ba-salt → reduced diphosphopyridine nucleotide. Y: 65-75%; purity 92%. A. L. Lehninger, Biochem. Prep. *2*, 92 (1952).

Nickel *Ni*

Amines from hydrazones $C{:}N{\cdot}NH_2 \rightarrow CHNH_2$

s. *9*, 444

Amines from nitriles $CN \rightarrow CH_2NH_2$

s. *9*, 270

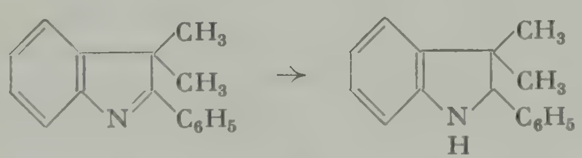
1,2,3,4-Tetrahydro- from 3,4-dihydro-isoquinolines $C{:}N \rightarrow CHNH$

s. *9*, 84

Palladium-carbon *Pd-C*

Indolines from pseudoindoles $C{:}N \rightarrow CHNH$

83.



2-Phenyl-3,3-dimethylpseudoindole hydrogenated with 10%-Pd-on-carbon in ethyl acetate → 2-phenyl-3,3-dimethylindoline. Y: 98%. B. Witkop, J. B. Patrick, and H. M. Kissman, B. *85*, 949 (1952).

1,2,3,4-Tetrahydro- from 3,4-dihydro-isoquinolines
s. *9*, 84

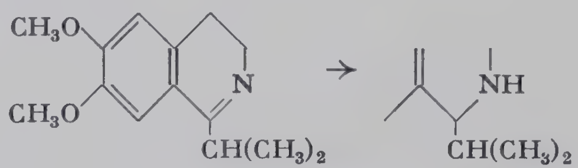
Platinum oxide *PtO_2*

Amines from nitriles $CN \rightarrow CH_2NH_2$
s. *1*, 53; s. a. J. Harley-Mason and A. H. Jackson, Soc. *1954*, 1165

Tert. amines from quaternary ammonium salts ←
s. *9*, 949

1,2,3,4-Tetrahydro- from 3,4-dihydro-isoquinolines $C{:}N \rightarrow CHNH$

84.



1-Isopropyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrogenated 1 hr. with PtO_2 or Pd-on-charcoal in ethanol at 3 atm. → 1-isopropyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (startg. m. f. 28). Y: 95%.— Hydrogenation of the hydrochlorides in ethanol or water requires 4-6 hrs. F. e. s. P. N. Craig et al., Am. Soc. *74*, 1316 (1952); with Raney-Ni at 100° and 100 atm. s. A. M. Barbier and P. Rumpf, Bl. *1953*, 293.

Addition to Sulfur and Carbon HC⇓SC

Lithium aluminum hydride *$LiAlH_4$*

Mercaptans from ethylenesulfides ⊂

85.

An ethereal soln. of butylthiacyclopropane added with stirring during 30 min. to a soln. of $LiAlH_4$ in anhydrous ether, and refluxed 2 hrs. → 2-hexanethiol. Y: 73%. F. e. s. F. G. Bordwell, H. M. Andersen, and B. M. Pitt, Am. Soc. *76*, 1082 (1954).

Addition to Carbon HC⇓CC

Sodium *Na*

Selective hydrogenation of condensed N-heterocyclic rings ←
s. *4*, 66; s. a. H. de Diesbach et al., Helv. *35*, 2322 (1952)

Sodium amalgam *Na,Hg*

Hydrogenation of ethylene derivatives C:C → CHCH

s. *3*, 610; s. a. G. R. Clemo and L. K. Mishra. Soc. *1953*, 192

Lithium/liq. ammonia *Li/NH$_3$*

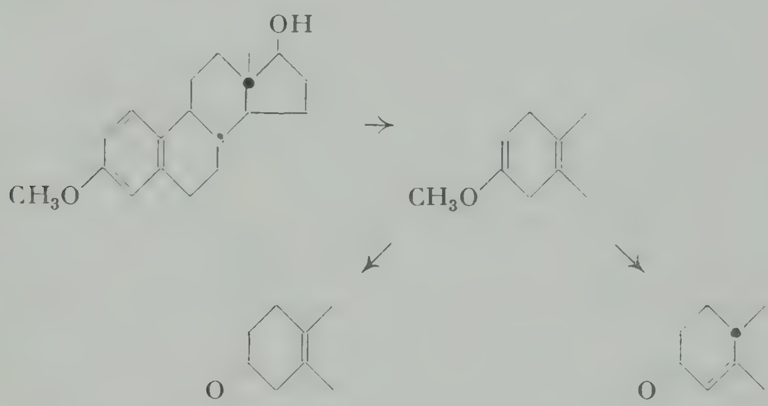
Ketones from ethyleneketones

s. *8*, 43; 3-ketosteroids from Δ^4-3-ketosteroids s. D. H. R. Barton, D. A. J. Ives, and B. R. Thomas, Soc. *1954*, 903

Lithium/liq. ammonia/alcohol *Li/NH$_3$/C$_2$H$_5$OH*

Cyclohexenones from phenolethers ←
Improved Birch reduction
Partial hydrogenation of isocyclics
Ketones from enolethers, also with migration of a carbon-carbon double bond

86.



Liq. NH_3 followed by Li-wire in small pieces added to a soln. of 3,17β-estradiol 3-methyl ether in ether, 10 min. later abs. alcohol added dropwise over a 10-20 min. period → 1,4-dihydro-3,17β-estradiol 3-methyl ether (Y: over 90%) dissolved in methanol

mixed with aq. oxalic acid, and allowed to stand 40 min. at 25° → 17β-hydroxy-5(10)-estren-3-one (Y: 83%).

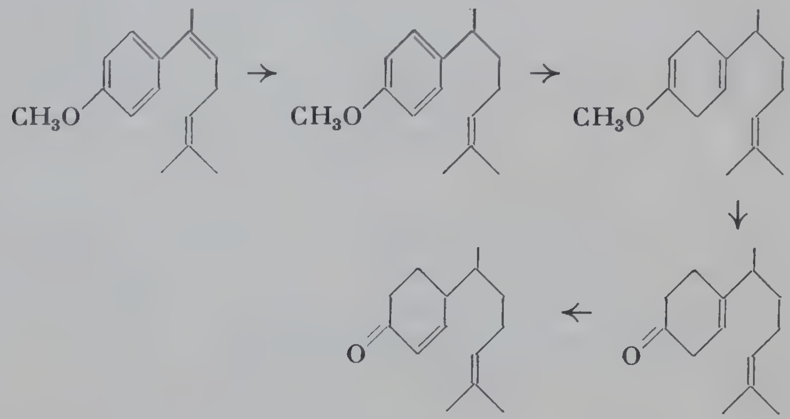
treated at 60° with 3 *N* HCl, and kept 15 min. more at the same temp. → 17β-hydroxy-4-estren-3-one (Y: ca. 88%). Over-all Y: 70-77%.

A. L. Wilds and N. A. Nelson. Am. Soc. *75*, 5366 (1953); f. e. of the reduction s. Am. Soc. *75*, 5360; s. a. C. Djerassi et al., Am. Soc. *76*, 4092 (1954).

Sodium/liq. ammonia/alcohol *$Na/NH_3/C_2H_5OH$*

Cyclohexenones from phenolethers
Birch reduction
Partial hydrogenation
of carbon-carbon bonds and isocyclics
Ketones from enolethers
α,β- from β,γ-Ethyleneketones

87.



39 g. 6-(p-Methoxyphenyl)-2-methyl-2,5-heptadiene in abs. alcohol added to liq. NH_3, then 25 g. Na added in small pieces during ca. 2.5 hrs., and stirring continued until the blue color is completely discharged → 6-(p-methoxyphenyl)-2-methyl-2-heptene (Y: 78%), 20 g. reduced with 20 g. Na as before → 6-(4′-methoxy-1′,4′-cyclohexadienyl)-2-methyl-2-heptene (Y: 85%) heated 35-40 min. with 5%-H_2SO_4 on a steam bath → 6-(4′-keto-1′-cyclohexenyl)-2-methyl-2-heptene (Y: 72%) dissolved in abs. alcohol, added dropwise to a soln. of Na in alcohol, warmed exactly 5 min. at 60°, then poured into crushed ice and acetic acid → 6-(4′-keto-2′-cyclohexenyl)-2-methyl-2-heptene (Y: 78%). S. M. Mukherji and N. K. Bhattacharyya, Am. Soc. *75*, 4698 (1953); 3-cyclohexenones from phenolethers s. a. G. Stork, S. S. Wagle, and P. C. Mukherji, Am. Soc. *75*, 3197 (1953).

Lithium aluminum hydride *$LiAlH_4$*

Nitroalkanes from nitroölefins C:C → CHCH

87a. $$C_3F_7CH{=}CHNO_2 \rightarrow C_3F_7CH_2CH_2NO_2$$

By *inverse addition* of $LiAlH_4$ to nitroolefins, nitroalkanes are obtained.—E: A soln. of $LiAlH_4$ in anhydrous ether added dropwise below −50° during 1.5 hrs. to a soln. of 3,3,4,4,5,5,5-heptafluoro-1-nitro-1-pentene in anhydrous ether, then allowed to come to room temp. → 1,1,1,2,2,3,3-heptafluoro-5-nitropentane. Y: 51%. F. e. s. D. J. Cook, O. R. Pierce, and E. T. McBee, Am. Soc. *76*, 83 (1954); method s. R. T. Gilsdorf and F. F. Nord, Am. Soc. *74*, 1837 (1952).

trans-Ethylene derivatives from acetylene derivatives C⋮C → CH:CH

s. 7, 91; s. a. K. R. Bharucha and B. C. L. Weedon, Soc. *1953*, 1584

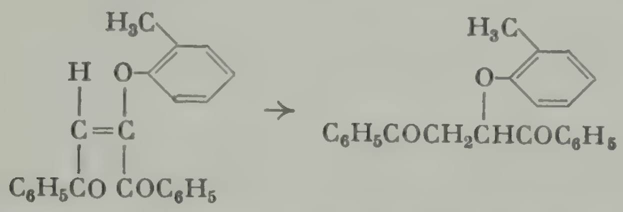
α,β-Ethylenealcohols from α,β-acetylenecarboxylic acids ←

s. *9*, 111

Hydrosulfite $S_2O_4^{--}$

γ-Diketones from α,β-ethylene-γ-diketones C:C → CHCH

88.



(2-Methylphenoxy)dibenzoylethylene refluxed 45 min. with Na-hydrosulfite in 75%-ethanol → (2-methylphenoxy)dibenzoylethane. Y: 93%. F. e. s. R. E. Lutz and S. M. King, J. Org. Chem. *17*, 1519 (1952).

Copper chromite $CuCr_2O_4$

Ring hydrogenation of isocyclics

s. *2*, 72; s. a. D. P. Phillips, Org. Synth. *34*, 31 (1954)

Cobaltic oxide/calcium oxide/sodium carbonate $Co_2O_3/CaO/Na_2CO_3$

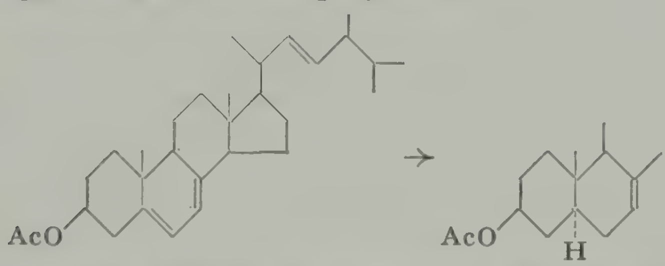
Ring hydrogenation of amines

s. *8*, 69; s. a. Am. Soc. *75*, 1156 (1953)

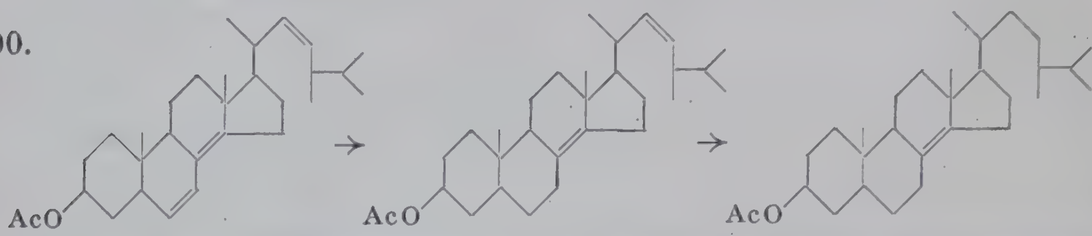
Nickel Ni

Partial hydrogenation of steroid polyenes

89.



A soln. of ergosteryl acetate in sulfur-free benzene treated with a suspension of Raney-Ni W 6 sludge (according to H. R. Billica and H. Adkins, Org. Synth. *29*, 25 (1949)) in benzene, and hydrogenated at 17° under slight positive pressure until a little more than the theoretical amount of H_2 has been absorbed → 5-dihydroergosteryl acetate. Y: 92-95%. R. C. Anderson, R. Stevenson, and F. S. Spring, Soc. *1952*, 2901.

90. 

A soln. of $\Delta^{6,8(14),22}$-ergostatrien-3β-ol acetate in dioxane hydrogenated at room temp. and atmospheric pressure with Raney-Ni (s. Synth. Meth. *1*, 56) previously satd. with H_2, until after ca. 3 hrs. the H_2-uptake ceases → $\Delta^{8(14),22}$-ergostadien-3β-ol acetate (Y: 98%) dissolved in anhydrous peroxide-free dioxane and hydrogenated with prereduced PtO_2 until after ca. 70 min. 1 mole H_2 has been absorbed → $\Delta^{8(14)}$-ergosten-3β-ol acetate (Y: ca. 100%). F. reductions with Raney-Ni s. G. D. Laubach and K. J. Brunings, Am. Soc. *74*, 705 (1952).

Ring hydrogenation of phenols

s. *4*, 76-8; s. a. K. W. Rosenmund and H. Herzberg, B. *87*, 1575 (1954)

Nickel-aluminum *Ni,Al*

Carboxylic acids from ethylenecarboxylic acids

s. *5*, 52; s. a. G. A. Page and D. S. Tarbell, Org. Synth. *34*, 8 (1954)

Nickel/chloroform *Ni/CHCl₃*

Ketones from ethyleneketones

91. $C_6H_5CH{=}CHCOCH_3 \rightarrow C_6H_5CH_2CH_2COCH_3$

Benzylideneacetone hydrogenated with Raney-Ni from 50%-alloy in the presence of chloroform (trace of HCl) → benzylacetone. Y: 86% as the oxime. R. Cornubert and J. Phélisse, Bl. *1952*, 403, 407, 410; prepn. of the catalyst s. Bl. *1952*, 399.

Nickel-silica *Ni-SiO₂*

Benzene ring hydrogenation

92. 

1,6-Diphenylhexane and Ni-kieselguhr catalyst in methylcyclohexane hydrogenated at 180-190° and 1700 p. s. i. → 1,6-dicyclohexylhexane. Y: 94%. F. e. s. K. T. Serijan and P. H. Wise, Am. Soc. *73*, 5191, 4766 (1951); s. a. J. H. Lamneck, Jr., and P. H. Wise, Am. Soc. *76*, 3475 (1954).

Ruthenium dioxide *RuO₂*

Ring hydrogenation of amines

93. A mixture of bis-(4-aminophenyl)methane, dioxane, and RuO_2 charged into an autoclave, repeatedly pressured to 200 lbs./sq. in. with H_2 and purged to remove air, then hydrogenated 4 hrs. at 100-120° and 166-200 atm. → bis-(4-aminocyclohexyl)methane. Y: 92%. A. E. Barkdoll et al., Am. Soc. *75*, 1156 (1953); formulas, cf. Synth. Meth. *8*, 69.

Palladium-calcium carbonate *Pd-CaCO₃*

Hydrogenation of acetylene derivatives ←

s. 9, 101

Palladium-barium sulfate *Pd-BaSO₄*

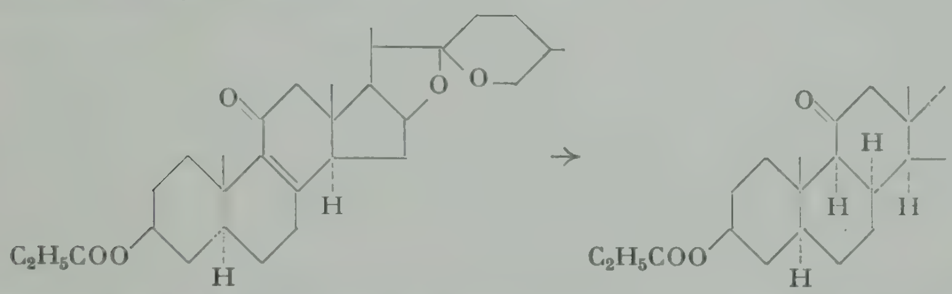
Hydrogenation of ethylene derivatives C:C → CHCH

s. 3, 46; of cinnamic acid esters s. J. R. Catch, H. P. W. Huggill, and A. R. Somerville, Soc. *1953*, 3028

Palladium-carbon *Pd-C*

Ketones from ethyleneketones
Stereochemistry of steroids

94.



A mixture of 0.5 g. Δ^8-22a-5α-spirosten-3β-ol-11-one propionate, 10%-Pd-carbon, and ethanol hydrogenated 20 hrs. at room temp. and atmospheric pressure → 0.35 g. 22a-5α-8-iso(α)-spirostan-3β-ol-11-one propionate.—Chemical reduction with Li in liq. NH_3 furnishes the trans(8β,9α)-isomer. F. e. s. C. Djerassi et al., Am. Soc. *75*, 3496 (1953).

Ethylene from acetylene derivatives C:C → CH:CH

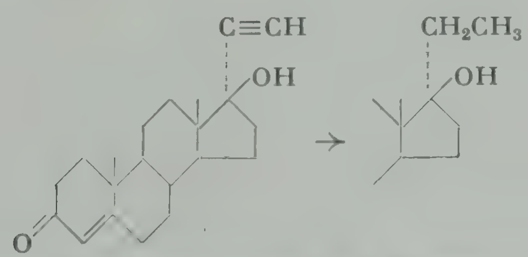
95.

$$CH_3OCH_2CH_2\overset{CH_3}{\underset{OH}{C}}\cdot C{\equiv}C\cdot CH_2OH \rightarrow CH_3OCH_2CH_2\overset{CH_3}{\underset{OH}{C}}\cdot CH{=}CHCH_2OH$$

6-Methoxy-4-methyl-2-hexyn-1,4-diol hydrogenated 2.5-3 hrs. with 17%-Pd-on-charcoal in abs. alcohol until 1 equivalent of H_2 has been absorbed → 6-methoxy-4-methyl-2-hexen-1,4-diol. Y: 75-85%. F. e. s. M. S. Newman, I. Waltcher, and H. F. Ginsberg, J. Org. Chem. *17*, 962 (1952).

Selective hydrogenation C⋮C → CH_2CH_2

96.



of acetylene derivatives. Hydrogenation can be performed selectively by suitable catalyst-solvent combinations.—E: A soln. of ethinyltesto-

sterone in purified dioxane hydrogenated with 5%-Pd-on-charcoal until the H_2-uptake practically ceases after 2 moles have been absorbed → 17-ethyltestosterone. Y: 80%. F. e. s. E. B. Hershberg et al., Am. Soc. *73*, 5073 (1951).

Palladium-carbon/sodium hydroxide *Pd-C/NaOH*

Carboxylic acids from α,β-ethylenecarboxylic acids C:C → CHCH

s. *8*, 75; s. a. M. B. Moore et al., Am. Soc. *76*, 3656 (1954)

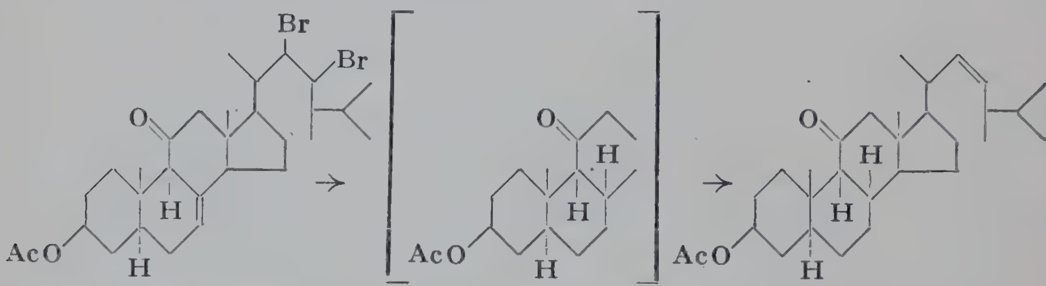
Platinum oxide *PtO_2*

Partial hydrogenation of steroid polyenes C:C → CHCH

s. *9*, 90

Hydrogenation of a carbon-carbon double bond with protection of another carbon-carbon double bond

97.



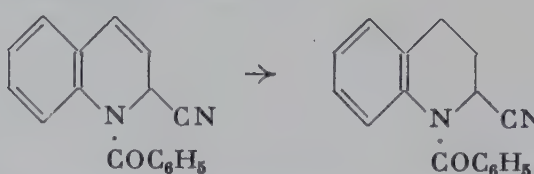
3β-Acetoxy-22,23-dibromo-9β-ergost-7-en-11-one in chloroform-acetic acid shaken 30 min. with PtO_2 under 100 atm. H_2, filtered, stirred and treated with Zn-dust during 1 hr. below 50°, and stirring continued at room temp. for 1 hr. → 3β-acetoxy-9β-ergost-22-en-11-one. Y: 74%. Also dechlorination s. J. Elks et al., Soc. *1953*, 2933.

Hydrocarbons from acetylene derivatives ←

s. *9*, 101

Selective hydrogenation of carbon-carbon double bonds in N-heterocyclics C:C → CHCH

98.



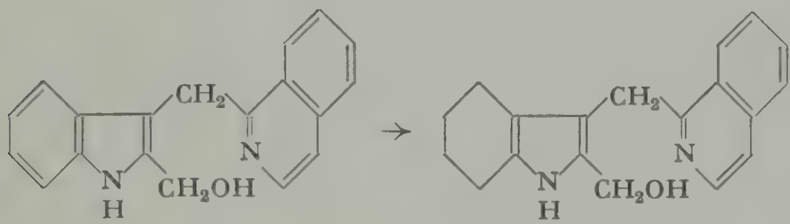
1-Benzoyl-1,2-dihydroquinaldonitrile and PtO_2 in 95%-ethanol hydrogenated at atmospheric pressure and room temp. until 1 molar equivalent of H_2 has been absorbed → 1-benzoyl-1,2,3,4-tetrahydroquinal-

donitrile. Y: 69%. F. e. s. W. E. McEwen, R. H. Terss, and I. W. Elliott, Am. Soc. *74*, 3605 (1952).

Hydrogenation of benzene rings

s. *9*, 931

Selective benzene ring hydrogenation of condensed N-heterocyclics



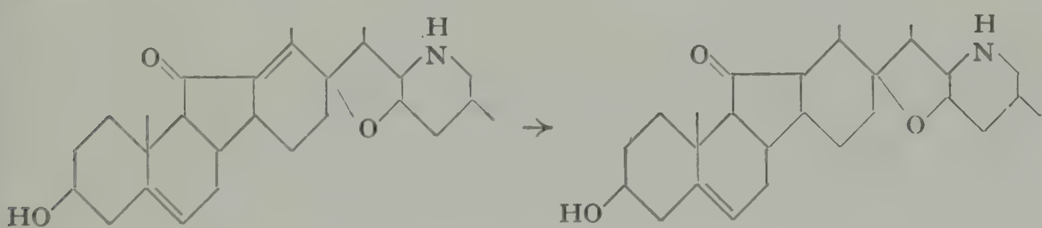
A soln. of 1-(2′-hydroxymethylskatyl)isoquinoline in glacial acetic acid hydrogenated with PtO_2 at room temp. and atmospheric pressure for 3 hrs. until 2 molar equivalents of H_2 have been absorbed → 1-(2′-hydroxymethyl-4′,5′,6′,7′-tetrahydroskatyl)isoquinoline. Y: 79%. V. Boekelheide and Chu-tsin Liu, Am. Soc. *74*, 4920 (1952); s. a. H. Schwarz and E. Schlittler, Helv. *34*, 629 (1951).

Ring hydrogenation of N-heterocyclics ←

s. *4*, 86; s. a. K. Winterfeld and C. Heinen, A. *578*, 171 (1952)

Platinum oxide/potassium hydroxide *PtO_2/KOH*

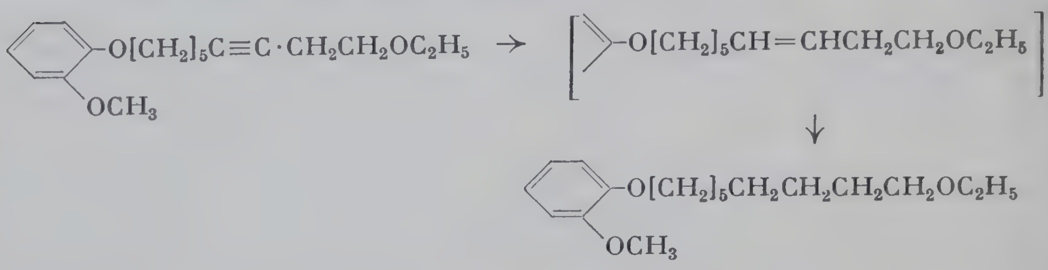
Partial and selective hydrogenation of carbon-carbon double bonds C:C → CHCH



PtO_2 prehydrogenated in alcohol, jervine and KOH in alcohol added, and hydrogenated 24 hrs. until the absorption of H_2 ceases → dihydrojervine. Y: 75%. R. Anliker, H. Heusser, and O. Jeger, Helv. *35*, 838 (1952); f. e. s. Helv. *35*, 936.

Via intermediates *v.i.*

Hydrogenation of acetylene derivatives C⋮C → CH_2CH_2

101. 

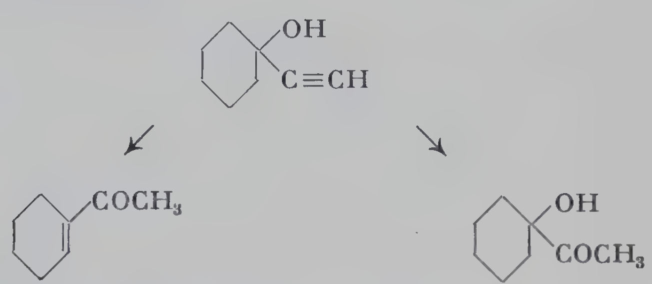
1-Ethoxy-9-o-methoxyphenoxynon-3-yne in ethyl acetate hydrogenated with 10%-Pd-on-$CaCO_3$ at room temp. and atmospheric pressure for 2 hrs. until the H_2-uptake ceases, the catalyst filtered off, PtO_2 added, and hydrogenation continued → 1-ethoxy-9-o-methoxyphenoxynonane. Y: 91%.—By this two-step procedure, hydrogenolysis of the ethoxy group, which may be caused by PtO_2, is avoided. F. e., in one step with PtO_2, s. A. W. Nineham, Soc. *1953*, 2601.

Rearrangement

Hydrogen/Oxygen Type HC ⌒ HO

Dowex-50 ←

Resins as catalysts ←
α,β-Ethyleneketones and α-hydroxyketones from α,β-acetylenealcohols

102. 

A mixture of 1-ethynylcyclohexanol,

Dowex-50 (a sulfonated polystyrene resin), acetic acid, and water refluxed 45 min. → 1-acetylcyclohexene. Y: 83.8-86.7%.

Hg-resin (Dowex-50 stirred into a soln. containing Hg-sulfate in dil. H_2SO_4), methanol, and water refluxed 4 hrs. → crude 1-acetylcyclohexanol. Y: 84%.

F. e. s. M. S. Newman, Am. Soc. *75*, 4740 (1953); with Zeo-Karb 225-Hg^{++} as Hg-resin s. J. D. Billimoria and N. F. Maclagan, Soc. *1954*, 3257.

Formic acid *HCOOH*

α,β-Ethyleneketones from α,β-acetylenealcohols ←
Rupe rearrangement

s. *5*, 508; s. a. H. H. Inhoffen and J. Kath, B. *87*, 1589 (1954)

Exchange

Oxygen ↑ HC⇅O

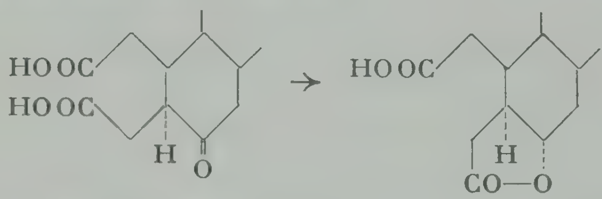
Sodium *Na*

Alcohols from carboxylic acid esters COOR → CH_2OH
Hansley modification of the
Bouveault-Blanc reduction

s. *3*, 49; choice of reducing alcohol s. a. G. Weitzel and J. Wojahn, H. *287*, 296 (1951)

Lactones from ketocarboxylic acids ○

103.



2.6 g. 6-keto-2,3-secocholestane-2,3-dicarboxylic acid in isopropyl alcohol treated with Na, whereby the Na-salt separates, ethanol added, and the mixture refluxed 2 hrs. with Na → 1.95 g. 6α-hydroxy-2,3-secocholestane-2,3-dicarboxylic acid 3 → 6α-lactone. C. W. Shoppee and G. H. R. Summers, Soc. *1952*, 3374; monocarboxylic acid without isopropyl alcohol s. D. Hoch and P. Karrer, Helv. *37*, 397 (1954).

Reduction of N-heterocyclics ←

s. *9*, 557

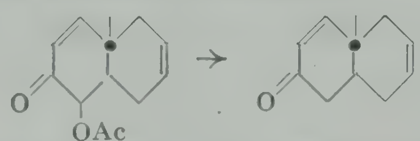
Lithium iodide/sodium boron hydride *LiI/NaBH₄*

s. Sodium boron hydride/lithium iodide

Zinc *Zn*

Replacement of acoxy groups by hydrogen OAc → H

104.



Crude *trans*-1-acetoxy-2-keto-10-methyl-$\Delta^{3,6}$-hexahydronaphthalene and acetic anhydride heated to boiling by immersion in an oil bath kept at 145-150°, commercial Zn-dust added all at once to the vigorously stirred soln., from which moisture is excluded, refluxing and stirring

continued for 8 min. → *trans*-2-keto-10-methyl-$\Delta^{3,6}$-hexahydronaphthalene. Y: 63%. R. B. Woodward et al., Am. Soc. *74*, 4223 (1952).

Zinc/sodium hydroxide *Zn/NaOH*

Hydrocarbons from quinones ←

s. *2*, 93; s. a. G. Wolf, Am. Soc. *75*, 2673 (1953)

Zinc amalgam/platinum oxide *Zn,Hg/PtO₂*

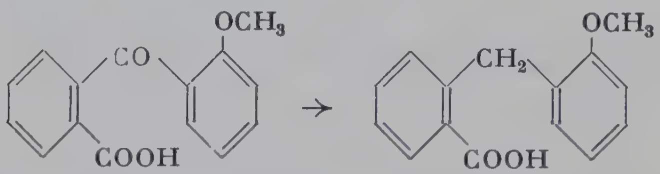
Hydrocarbons from acyloins $COCH(OH) \rightarrow CH_2CH_2$

s. *9*, 931; without subsequent hydrogenation cf. H. H. Günthard, S. D. Heinemann, and V. Prelog, Helv. *36*, 1147 (1953)

Zinc/cupric sulfate/ammonia *$Zn/CuSO_4/NH_3$*

Hydrocarbons from ketones $CO \rightarrow CH_2$

105.

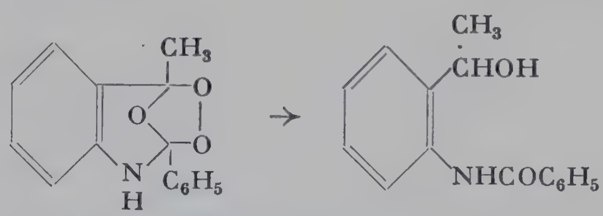


Zn-dust and a few drops of an ammoniacal soln. of $CuSO_4$ added to a soln. of o-(o-methoxybenzoyl)benzoic acid in aq. NH_3 and heated 20 hrs. at 100° with agitation → o-(o-methoxybenzyl)benzoic acid. Y: 75%.—A 2-step procedure (s. 366) is used for compounds containing halogen, which may be eliminated in the above process. F. e. s. E. D. Bergmann and E. Loewenthal, Bl. *1952*, 66.

Sodium boron hydride *$NaBH_4$*

Reductive cleavage of N-heterocyclic ozonides ←

106.



An alc. soln. of 500 mg. 2-phenylskatole ozonide slowly added at 0° to $NaBH_4$ in alcohol, more alcohol added, and refluxed 1 hr. → 440 mg. (o-benzamidophenyl)methylcarbinol. B. Witkop and J. B. Patrick, Am. Soc. *74*, 3855 (1952).

Sodium boron hydride/lithium iodide *$NaBH_4/LiI$*

Diols from ketocarboxylic acid esters ←

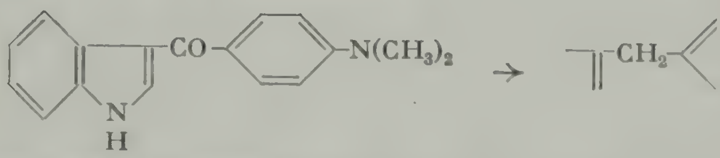
s. *9*, 876

Lithium aluminum hydride *$LiAlH_4$*

Ethylenimines from 2-alkoxyethylenimines OR → H
s. *9*, 242

Hydrocarbons from oxo compounds CO → CH_2

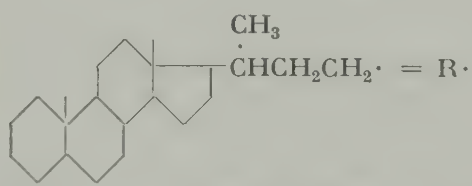
07.



A suspension of 3-(p-dimethylaminobenzoyl)indole in abs. ether stirred and treated with 5 moles 1 *M* ethereal $LiAlH_4$, then refluxed 4 hrs. → N,N-dimethyl-p-skatylaniline. Y: 83.4%. J. Thesing, H. Mayer, and S. Klüssendorf, B. *87*, 901 (1954); s. a. E. Leete and L. Marion, Can. J Chem. *31*, 457 (1953).

Hydrocarbons from carboxylic acids via alcohols and halides COOH → CH_3

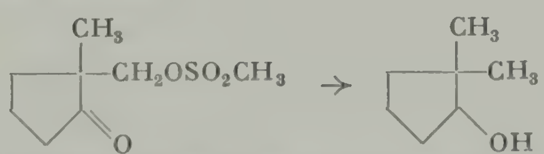
08. $R{\cdot}COOH \rightarrow R{\cdot}CH_2OH \rightarrow R{\cdot}CH_2Cl \rightarrow R{\cdot}CH_3$



Cholanic acid allowed to react with $LiAlH_4$ in ether in a Soxhlet apparatus → 24-hydroxycholane (Y: 94%) dissolved in a mixture of benzene and dimethylaniline, $SOCl_2$ added dropwise, and heated 0.5 hr. on a water bath → 24-chlorocholane (Y: 86%) dissolved in tetrahydrofuran, treated with $LiAlH_4$, and refluxed 10 hrs. → cholane (Y: 83%). F. reductions of carboxylic acids s. F. Wessely and W. Swoboda, M. *82*, 437 (1951); via bromides, which are reduced with Zn/CH_3COOH, s. S. F. Birch et al., Soc. *1952*, 1363; reduction with Raney-Ni s. C. A. Grob and E. Renk, Helv. *37*, 1689 (1954).

Hydrocarbons from methylsulfonic acid esters ←
Sec. alcohols from ketones

09.



A soln. of 2-hydroxymethyl-2-methylcyclopentanone mesylate in abs. ether added during 45 min. at 0° to $LiAlH_4$, ca. ¾ of the ether evaporated, then refluxed 3 hrs. → 2,2-dimethylcyclopentanol. Y: 89%. A. Eschenmoser and A. Frey, Helv. *35*, 1660 (1952).

Hydrocarbons from p-toluenesulfonic acid esters OTs → H

s. *6*, 47; *8*, 88; s. a. P. Karrer and R. Saemann, Helv. *35*, 1932 (1952); partial reduction s. P. Karrer and E. Vis, Helv. *37*, 378 (1954)

Alcohols from carboxylic acid esters COOR → CH_2OH

s. *6*, 101; s. a. A. Campbell and H. N. Rydon, Soc. *1953*, 3002

Hydroxyacetals from carbalkoxyacetals

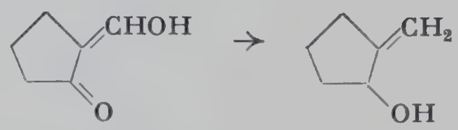
s. *8*, 91; s. a. C. D. Hurd and W. H. Saunders, Jr., Am. Soc. *74*, 5324 (1952)

Alcohols from acyl peroxides $(RCOO)_2 \rightarrow 2\,RCH_2OH$

s. *9*, 6

Reduction of enolizable β-dioxo compounds to ethylenealcohols ←

110.



Solid 2-hydroxymethylenecyclopentanone added to a soln. of $LiAlH_4$ in dry ether → 2-methylenecyclopentanol. Y: 57%. F. e., also reduction of β-ketocarboxylic acid esters, s. A. S. Dreiding and J. A. Hartman, Am. Soc. *75*, 939 (1953).

2-Ethylenealcohols from α,β-acetylenecarboxylic acids ←

111. $$HOOC\cdot C\equiv C\cdot COOH \rightarrow HOCH_2CH{=}CHCH_2OH$$

An ethereal soln. of acetylenedicarboxylic acid added dropwise with stirring to an ethereal soln. of $LiAlH_4$ under N_2, and stirring continued 16 hrs. at room temp. → 2-butene-1,4-diol. Y: 84%.—Similarly: Propiolic acid → allyl alcohol. Y: 85%. G. E. Benedict and R. R. Russell, Am. Soc. *73*, 5444 (1951).

Diols from carboxylic acid anhydrides ←

s. *7*, 105; s. a. W. J. Bailey, J. Rosenberg, and L. J. Young, Am. Soc. *76*, 2251 (1954)

Aldehydes from carboxylic acids and esters COOR → CHO
Inverse addition

112. $$C_2F_5COOR \rightarrow C_2F_5CHO$$

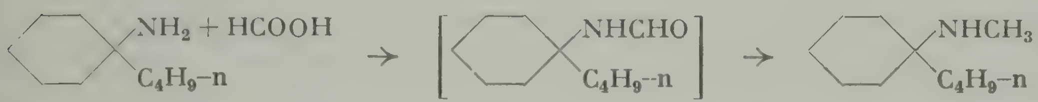
$LiAlH_4$ in ether added dropwise with stirring at –70° to perfluoropropionic ester, and the product isolated after 3 hrs. → perfluoropro-

pionaldehyde. Y: 75%. F. e. s. O. R. Pierce and T. G. Kane. Am. Soc. *76*, 300 (1954); from carboxylic acids s. M. Braid, H. Iserson, and F. E. Lawlor, Am. Soc. *76*, 4027 (1954).

Amines from carboxylic acid amides $CON\langle \rightarrow CH_2N\langle$

s. *9*, 524; s. a. O. Klamerth and W. Kutscher, B. *85*, 444 (1952); V. M. Mićović and M. L. Mihailović, J. Org. Chem. *18*, 1190 (1953); with Soxhlet extractor s. J. Swidinsky, F. H. McMillan, and J. A. King, Am. Soc. *76*, 1148 (1954)

Alkylation of amines
N-Methylation

13.


A mixture of 1-n-butylcyclohexylamine and 98%-formic acid heated 2 hrs. at 180-190°, the dry ethereal soln. of the crude product added dropwise to ethereal $LiAlH_4$, refluxed 6 hrs., and the final product isolated as the sesquioxalate → 1-n-butyl-N-methylcyclohexylamine sesquioxalate. Y: 83%. F. e. and methods s. K. E. Hamlin and M. Freifelder, Am. Soc. *75*, 369 (1953); s. a. F. F. Blicke and Chi-Jung Lu, Am. Soc. *74*, 3933 (1952).

Cyclic imines from dicarboxylic acid imides ←

s. *6*, 103; s. a. D. Hoch and P. Karrer, Helv. *37*, 397 (1954); L. M. Rice, E. E. Reid, and C. H. Grogan, J. Org. Chem. *19*, 884 (1954)

Methylamines from isocyanates $N{:}C{:}O \rightarrow NHCH_3$

s. *8*, 95; s. a. W. Ried and F. Müller, B. *85*, 470 (1952)

Aminoalcohols from
dicarboxylic acid monoamides and
dicarboxylic acid amide esters ←

14. $$(CH_3)_2NCOCH_2CH_2COOH \rightarrow (CH_3)_2NCH_2CH_2CH_2CH_2OH$$

23.3 g. N,N-dimethylsuccinamic acid extracted by means of a Soxhlet apparatus into a boiling soln. of $LiAlH_4$ in dry ether with stirring over a period of 18 hrs. → 11.3 g. 4-dimethylamino-1-butanol. Also from amide esters s. A. W. D. Avison, J. Applied Chem. *1*, 469 (1951).

Aluminum alkoxide *Al(OR)₃*

Meerwein-Ponndorf-Verley reduction
Lactones from ketocarboxylic acids ○

115. $$C_{11}H_{23}COCH_2CH_2COOH \rightarrow \begin{array}{l} C_{11}H_{23}CHCH_2CH_2CO \\ \quad\ \llcorner O \text{———}\lrcorner \end{array}$$

4-Ketopentadecanoic acid and Al-isopropoxide in isopropanol slowly distilled through a Fenske column until no more acetone distills off → 4-hydroxypentadecanoic lactone. Y: 93%. R. E. Bowman and W. D. Fordham, Soc. *1951*, 2753.

Formic acid/formaldehyde *$HCOOH/H_2CO$*

Methylamines from formamides $NCHO \rightarrow NCH_3$

116. $$\begin{array}{l} (C_6H_5)_2C\cdot CN \\ \quad\quad\ | \\ CH_3CHCH_2N \begin{array}{l} \diagup CHO \\ \diagdown CH_3 \end{array} \end{array} \rightarrow \begin{array}{l} (C_6H_5)_2C\cdot CN \\ \quad\quad\ | \\ CH_3CHCH_2N \begin{array}{l} \diagup CH_3 \\ \diagdown CH_3 \end{array} \end{array}$$

A mixture of 4-methylformamido-2,2-diphenyl-3-methylbutanenitrile, trioxane, and 98-100%-formic acid refluxed 112 hrs. → 4-dimethylamino-2,2-diphenyl-3-methylbutanenitrile. Y: 91%. M. Sletzinger, E. M. Chamberlin, and M. Tishler, Am. Soc. *74*, 5619 (1952).

Hydrosulfite *$S_2O_4^{--}$*

Anthrones from anthraquinones $CO \rightarrow CH_2$
s. *6*, 106; also limitations s. W. Bradley and R. F. Maisey, Soc. *1954*, 274

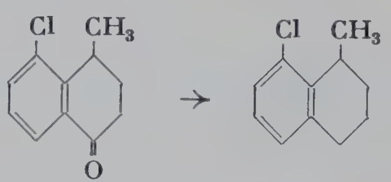
Copper chromite *$CuCr_2O_4$*

Alcohols from carboxylic acid esters $COOR \rightarrow CH_2OH$
selective reduction s. *9*, 567; optically active compounds s. E. Segel, Am. Soc. *74*, 1096 (1952)

Palladium-barium sulfate *$Pd\text{-}BaSO_4$*

Hydrocarbons from ketones $CO \rightarrow CH_2$

117.

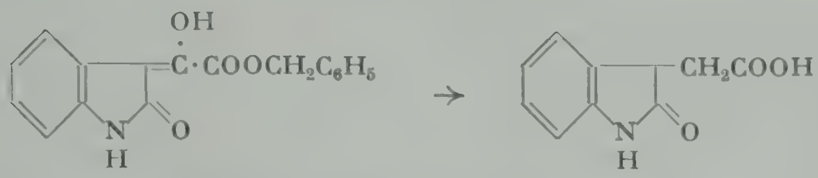


A soln. of 4-methyl-5-chloro-1-tetralone in 95%-ethanol hydrogenated with 5%-$Pd\text{-}BaSO_4$ at room temp. and 3 atm. until 2 molar equivalents of H_2 have been absorbed → 1-methyl-8-chloro-1,2,3,4-tetrahydronaphthalene (startg. m. f. 898). Y: 75%. J. Cason and D. D. Phillips, J. Org. Chem. *17*, 298 (1952).

Palladium-carbon *Pd-C*

Carboxylic acids from α,β-ethylene-α-hydroxycarboxylic acid esters C:C(OH)COOR → $CHCH_2COOH$

8.



A soln. of benzyl isatylidenehydroxyacetate in a mixture of glacial acetic acid and concd. H_2SO_4 shaken with 10%-Pd-on-charcoal under 3-4 atm. of H_2 until 3 molar equivalents have been absorbed, filtered onto Na-acetate, and the solvent removed in vacuo with mild heating → oxindole-3-acetic acid. Y: 70%. P. L. Julian et al., Am. Soc. *75*, 5305 (1953).

Platinum oxide/zinc amalgam *PtO_2/Zn,Hg*

s. Zinc amalgam/platinum oxide

Via intermediates *v.i.*

Hydrocarbons from oxo compounds via hydrazones Wolff-Kishner reduction CO → CH_2

without addition of alkali

s. *3*, 58; *5*, 66; in amyl alcohol s. H. Kloosterziel, W. van der Veen, and H. J. Backer, R. *71*, 1231 (1952)

Simplified procedure

s. *2*, 96; s. a. M. *83*, 865 (1952)

Huang-Minlon reduction

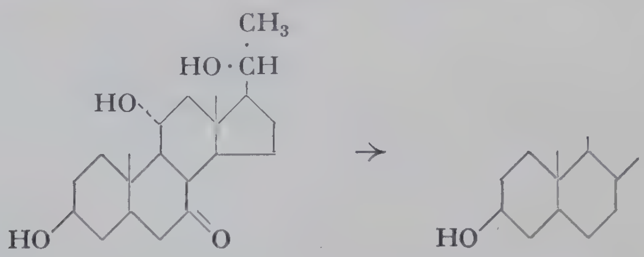
with preceding acid cleavage

s. *9*, 228

19. $C_{11}H_{23}COCH_2CH_2CH(OC_2H_5)_2 \rightarrow C_{11}H_{23}CH_2CH_2CH_2CH(OC_2H_5)_2$

Acetals from ketoacetals. 4-Ketopentadecan-1-al diethyl acetal, KOH, hydrazine hydrate, and 2,2′-dihydroxydiethyl ether refluxed 1.5 hrs., the temp. raised to 200° by distillation, and kept at that temp. for a further 4 hrs. → n-pentadecanal diethyl acetal. Y: 90%. R. E. Bowman and W. D. Fordham, Soc. *1951*, 2758.

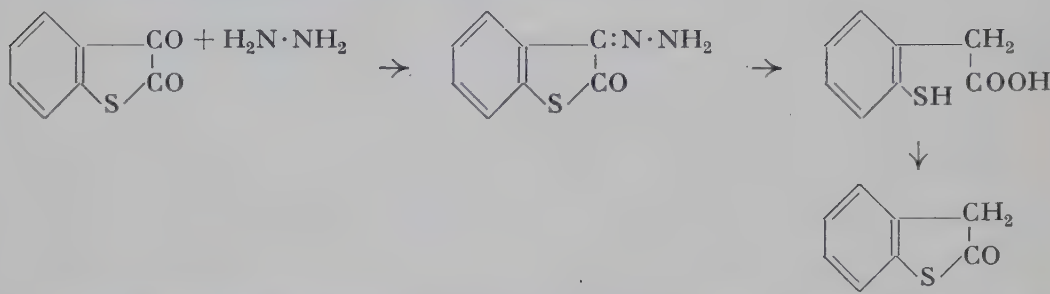
120.



Two-step procedure. 0.73 g. allopregnane-3β,11α,20β-triol-7-one refluxed 1 hr. with ethylene glycol and hydrazine hydrate, aq. KOH added, heated without condenser until the vapor temp. has reached 190°, then refluxed 4 hrs. → 0.59 g. allopregnane-3β,11α,20β-triol. C. Djerassi et al., Am. Soc. *75*, 3505 (1953).

Thioöxindoles from thianaphthenequinones via o-mercaptophenylacetic acids ←

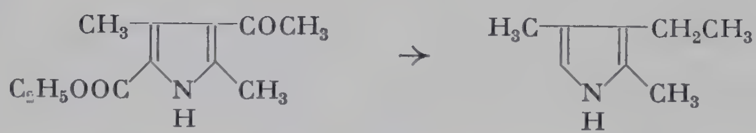
121.



Hydrazine hydrate added slowly to a boiling soln. of thianaphthenequinone in a minimum of ethanol, and refluxed 15 min. → thianaphthenequinone 3-hydrazone (Y: 67%) dissolved in aq. 25%-KOH, and gently refluxed 16 hrs. → o-mercaptophenylacetic acid (Y: 84%), steam-distilled in aq. HCl → thioöxindole (startg. m. f. 857) (Y: 87%). F. e. s. R. H. Glauert and F. G. Mann, Soc. *1952*, 2127.

Simplified Wolff-Kishner reduction with simultaneous decarbalkoxylation Decarboxylation by azeotropic distillation Pyrroles CO → CH_2

122.



A mixture of ethyl 3,5-dimethyl-4-acetyl-2-pyrrolecarboxylate, NaOH, hydrazine hydrate, and triethylene glycol refluxed 2 hrs., the alcohol formed distilled off through a column, water added dropwise when the temp. has reached 180°, and the product distilled azeotropically with addition of a trace of Silikon SH (Wacker) to prevent foaming → cryptopyrrole. Y: over 80%.—Also decarbalkoxylation without reduction in the presence of a little hydrazine hydrate to stabilize the pyrrole derivatives, s. A. Treibs and R. Schmidt, A. *577*, 105 (1952).

Reduction of oxo- to hydrocarbon groups with simultaneous formation of amines from nitro compounds

123.

2′-Nitro-2,3:6,7-dibenzocyclohepta-2,4.6-trien-1-one and hydrazine hydrate added to a soln. of KOH in trimethylene glycol, refluxed 1.5 hrs. under N_2, the condenser removed, heating in a N_2-stream continued until the boiling temp. reaches 200-205°, finally refluxed 5 hrs. at this temp. → 2′-amino-2,3:6,7-dibenzocyclohepta-2,4,6-triene. Y: 79-81%. T. W. Campbell, R. Ginsig, and H. Schmid, Helv. *36*, 1489 (1953).

Hydrocarbons from ketones via mercaptals

s. *7*, 116; s. a. H. M. Walborsky and E. R. Buchman, Am. Soc. *75*, 6339 (1953)

Nitrogen ↓ HC⇅N

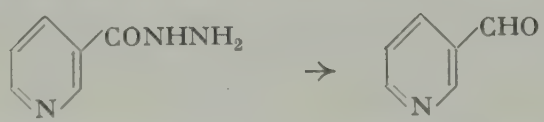
Irradiation/alkyl nitrite ←

s. Alkyl nitrite/irradiation

Sodium *Na*

Aldehydes from carboxylic acid hydrazides $CONHNH_2 \rightarrow CHO$

124.



A soln. of crude nicotinyl hydrazide in aq. NH_3 added to a stirred ice-cold soln. of Na-metaperiodate in aq. NH_3 as rapidly as the gas evolution permits, stirring and cooling continued for 5 min., allowed to stand for 15 more min., treated with aq. Ba-acetate, and filtered → nicotinaldehyde. Crude Y: 60-70%. H. N. Wingfield, W. R. Harlan, and H. R. Hanmer, Am. Soc. *74*, 5796 (1952).

Sodium amalgam *Na,Hg*

Reductive cleavage of quaternary ammonium salts $CH_2\overset{+}{N}\langle \rightarrow CH_3$

Emde degradation

s. *8*, 105; s. a. Org. Synth. *34*, 56 (1954)

Potassium hydroxide *KOH*

o-Mercaptophenylacetic acids from thianaphthenequinone 3-hydrazones

s. *9*, 121

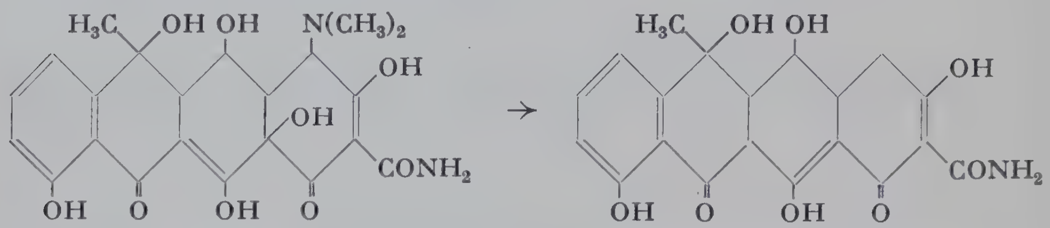
Zinc *Zn*

Hydrocarbons from diazonium fluoborates $N_2^+ \rightarrow H$

s. *9*, 129

Zinc/acetic acid *Zn/CH_3COOH*

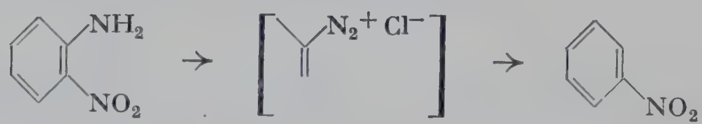
Tetracycline derivatives ←
Simultaneous elimination of tert-amino- and hydroxyl groups

125.


Terramycin, Zn, and acetic acid stirred 4 days at 25-30° → desdimethylaminodesoxyterramycin. Y: 50%. F. A. Hochstein et al., Am. Soc. *75*, 5455 (1953); **reductive deamination** s. a. J. H. Brewster and M. W. Kline, Am. Soc. *74*, 5179 (1952).

Alkyl nitrite/irradiation ←

Replacement of amino groups by hydrogen $NH_2 \rightarrow H$

126.


Photoreduction. o-Nitraniline diazotized with ethyl nitrite in isopropanol in the presence of a small excess of HCl, then irradiated with UV-light at 0° for 3-4 hrs. → nitrobenzene. Y: 75%. Isopropanol is particularly suitable as medium due to its favorable reduction-oxidation properties. F. e., also with isolation of the diazonium salts, s. L. Horner and H. Stöhr, B. *85*, 993 (1952).

Hypophosphorous acid *H_3PO_2*

Diazotization in the presence of hypophosphorous acid

at ca. 5° s. *5*, 67; at ca. 35° s. R. A. Henry and W. G. Finnegan, Am. Soc. *76*, 290 (1954)

Hypophosphorous acid/cupric sulfate *$H_3PO_2/CuSO_4$*

s. *7*, 119

Hydrochloric acid *HCl*

Cleavage of azosulfonylthioethers $N{:}NR \rightarrow H$

s. *9*, 140

Nickel *Ni*

Hydrogenolysis of Mannich bases $NR_2 \rightarrow H$

127. $(C_6H_5)_2CHCOCH_2CH_2N(CH_3)_2 \rightarrow (C_6H_5)_2CHCOCH_2CH_3$

4-Dimethylamino-1,1-diphenyl-2-butanone hydrochloride hydrogenated with Raney-Ni in abs. ethanol at 80° and an initial pressure of 1180 p. s. i. for 2.5 hrs. until 1 molar equivalent of H_2 has been absorbed → 1,1-diphenyl-2-butanone. Y: 72%. F. e. s. E. M. Schultz and J. B. Bicking, Am. Soc. *75*, 1128 (1953).

Palladium-carbon *Pd-C*

Amines from diazo compounds with simultaneous replacement of halogen by hydrogen ←

s. *9*, 876

Platinum oxide *PtO_2*

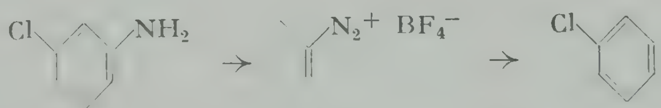
Hydrogenolysis of unsatd. quaternary ammonium salts ←

128. $n\text{-}C_4H_9CH{=}CHCH_2\overset{+}{N}(CH_3)_3\ I^- \rightarrow n\text{-}C_4H_9CH_2CH_2CH_3$

14.15 g. 2-n-heptenyltrimethylammonium iodide hydrogenated with PtO_2 in ethanol at 15-19° → 3.2 g. n-heptane.—3-Unsatd. salts are hydrogenated without hydrogenolysis. F. e. s. R. Epsztein, M. Olomucki, and J. Marszak, Bl. *1952*, 777.

Via intermediates *v.i.*

Replacement of amino groups by hydrogen via diazonium fluoborates $NH_2 \rightarrow H$

129. 

m-Chloroaniline diazotized in aq. HBF_4 with $NaNO_2$, and cooled by addition of Dry Ice before filtration → m-chlorobenzenediazonium fluoborate (Y: 98%) added slowly to abs. ethanol and Zn-dust at a rate to maintain gentle reflux, which is continued 1 hr. after the addition → chlorobenzene (Y: 82.6%). F. e. s. A. Roe and J. R. Graham, Am. Soc. *74*, 6297 (1952).

Carboxylic acids from α-hydroxylactams via ketocarboxylic acids C

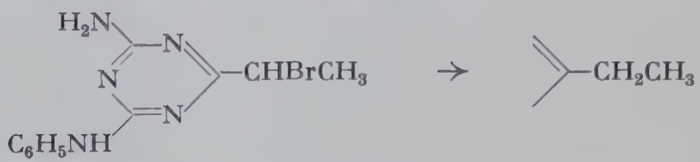
s. *9*, 744

Halogen ↑ HC ⇅ Hal

Sodium iodide/acetic acid *NaI/CH_3COOH*

Replacement of halogen by hydrogen Hal → H

130.



A soln. of 2-α-bromoethyl-4-amino-6-anilino-*s*-triazine in acetone added to a soln. of NaI in acetone and a little acetic acid, allowed to stand overnight → 2-ethyl-4-amino-6-anilino-*s*-triazine. Y: 88.7%. F. e. and comparison with Pd-$CaCO_3$ hydrogenation s. S. L. Shapiro and C. G. Overberger, Am. Soc. *76*, 97 (1954); method s. A. H. Blatt and E. W. Tristram, Am. Soc. *74*, 6273 (1952).

Copper *Cu*

Replacement of chlorine by hydrogen Cl → H

s. *6*, 118; s. a. E. V. Brown, Am. Soc. *76*, 3167 (1954)

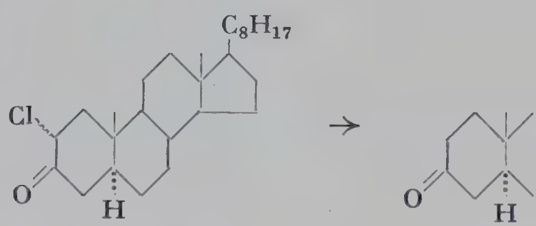
Zinc/acetic acid *Zn/CH_3COOH*

Replacement of halogen by hydrogen Hal → H

s. *9*, 108

Replacement of chlorine by hydrogen Cl → H
Activated zinc

131.



A mixture of 0.257 g. 2-chloro-3-cholestanone, activated Zn (prepn. s. original paper), and glacial acetic acid refluxed 10 hrs. → 0.225 g. 3-cholestanone.—The reduction was not successful with ordinary Zn-dust or $CrCl_2$. J. J. Beereboom et al., Am. Soc. *75*, 3500 (1953).

Zinc/hydrochloric acid *Zn/HCl*

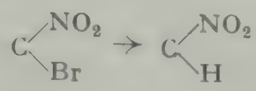
Selective replacement of iodine by hydrogen I → H

132. $CF_3CI{=}CHCCl_3 \rightarrow CF_3CH{=}CHCCl_3$

1,1,1-Trichloro-4,4,4-trifluoro-3-iodo-2-butene refluxed 3 hrs. with Zn and dil. HCl → 1,1,1-trichloro-4,4,4-trifluoro-2-butene (startg. m. f. 329). Y: 63%. R. N. Haszeldine, Soc. *1953*, 922.

Sodium boron hydride *$NaBH_4$*

Aliphatic nitro compounds from 1,1-bromonitro compounds



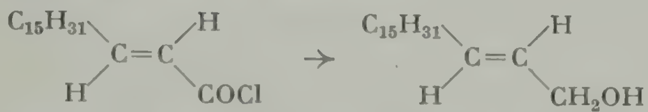
s. *9*, 168

Lithium aluminum hydride *$LiAlH_4$*

Replacement of halogen by hydrogen Hal → H

s. *9*, 108

2-Ethylenealcohols from α,β-ethylenecarboxylic acid chlorides COCl → CH_2OH

133. 

An ethereal soln. of 12% excess $LiAlH_4$ added dropwise at –20° to an ethereal soln. of *trans*-2-octadecenoic acid chloride, stirring continued 1 hr. at –16° and 30 min. at 20° → *trans*-2-octadecen-1-ol. Y: 80%.— The free acid and the ester give mostly the saturated alcohol. E. F. Jenny and C. A. Grob, Helv. *36*, 1936 (1953).

Ethyl alcohol *C_2H_5OH*

Disproportionation ←

134. $(p\text{-}CH_3OC_6H_4)_2CHCl + CH_3CH_2OH \rightarrow (p\text{-}CH_3OC_6H_4)_2CH_2 + CH_3CHO$

A soln. of di-(p-methoxyphenyl)methyl chloride in 96%-ethanol refluxed 6 hrs. in a slow CO_2-stream → di-(p-methoxyphenyl)methane (Y: 80%) and acetaldehyde (Y: 75% as the 2,4-dinitrophenylhydrazone). F. e. with alcohols s. M. P. Balfe, J. Kenyon, and E. M. Thain. Soc. *1952*, 790.

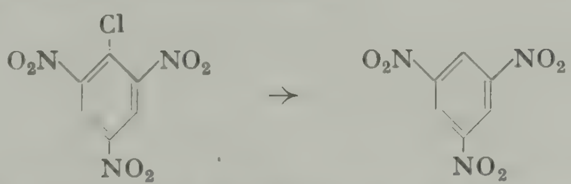
Chromous chloride *$CrCl_2$*

Replacement of halogen by hydrogen Hal → H

s. *4*, 112; s. a. J. J. Beereboom and C. Djerassi, J. Org. Chem. *19*, 1196 (1954)

Hydriodic acid *HI*

Replacement of chlorine by hydrogen Cl → H

135. 

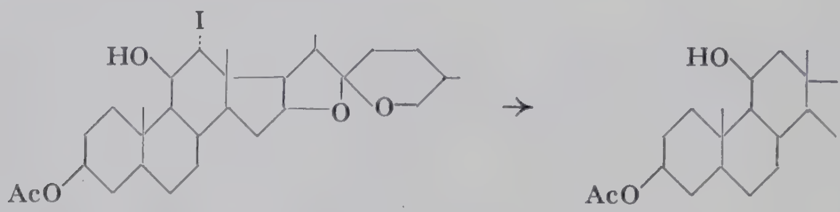
A soln. of picryl chloride in acetone added to a soln. of NaI in acetone containing acetic acid, allowed to stand 24 hrs. at room temp., then

poured into aq. $NaHSO_3$ → trinitrobenzene. Y: 60% (crude Y: up to 100%). A. H. Blatt and E. W. Tristram, Am. Soc. *74*, 6273 (1952); purine derivatives s. R. K. Robins and B. E. Christensen, Am. Soc. *74*, 3624 (1952).

Nickel *Ni*

Replacement of iodine by hydrogen I → H

136.

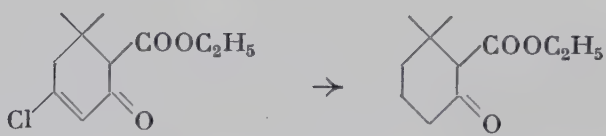


Raney-Ni satd. with H_2 added to a soln. of 3β-acetoxy-11β-hydroxy-12α-iodo-5α,22a-spirostane in dioxane-ether and stirred 23 hrs. at 0-5° in the dark → 3β-acetoxy-11β-hydroxy-5α,22a-spirostane. Y: 93.0%. J. Schmidlin and A. Wettstein, Helv. *36*, 1241 (1953).

Palladium-calcium carbonate/pyridine *$Pd\text{-}CaCO_3/C_5H_5N$*

Hydrocarbons from α,β-ethylenechlorides C:CCl → $CHCH_2$
Selective hydrogenation

137.



Ethyl 5-chloro-1,1-dimethyl-3-oxo-4-cyclohexene-2-carboxylate hydrogenated in alcohol with prehydrogenated 2,5%-Pd-$CaCO_3$ in the presence of pyridine until 10% more than the calculated amount of H_2 has been absorbed → ethyl 1,1-dimethylcyclohexan-3-one-2-carboxylate. Y: 90%. U. Steiner and B. Willhalm, Helv. *35*, 1752 (1952); f. e. s. H. Favre and H. Schinz, Helv. *35*, 2388 (1952).

Palladium-strontium carbonate *$Pd\text{-}SrCO_3$*

Replacement of halogen by hydrogen Hal → H

s. *7*, 128; s. a. B. H. Chase and J. Walker, Soc. *1953*, 3548

Palladium-barium sulfate *$Pd\text{-}BaSO_4$*

Aldehydes from carboxylic acid chlorides COCl → CHO

s. *1*, 100/1; s. a. K. Freudenberg and H. H. Hübner, B. *85*, 1181 (1952); J. P. Lambooy, Am. Soc. *76*, 133 (1954); K. Balenović et al., J. Org. Chem. *18*, 297 (1953)

Palladium-barium sulfate/calcium carbonate *Pd-BaSO₄/CaCO₃*

Replacement of bromine by hydrogen Br → H

138.

$$\begin{array}{c} COOCH_3 \\ \cdot \\ CH_2 \\ \cdot \\ HC\cdot COOCH_3 \\ \cdot \\ CH_2 \\ \cdot \\ BrCH \\ \cdot \\ COOCH_3 \end{array} \rightarrow \begin{array}{c} COOCH_3 \\ \cdot \\ CH_2 \\ \cdot \\ HC\cdot COOCH_3 \\ \cdot \\ CH_2 \\ \cdot \\ CH_2 \\ \cdot \\ COOCH_3 \end{array}$$

H_2 passed at 60° through a mixture of trimethyl δ-bromo-β-carboxyadipate, Pd-$BaSO_4$, $CaCO_3$, and 90%-methanol, as long as CO_2 is formed → trimethyl β-carboxyadipate. Y: 85%. K. Freudenberg and J. Geiger, A. *575*, 145 (1952).

Palladium-carbon *Pd-C*

Replacement of halogen by hydrogen ←
simultaneously amines from diazo compounds

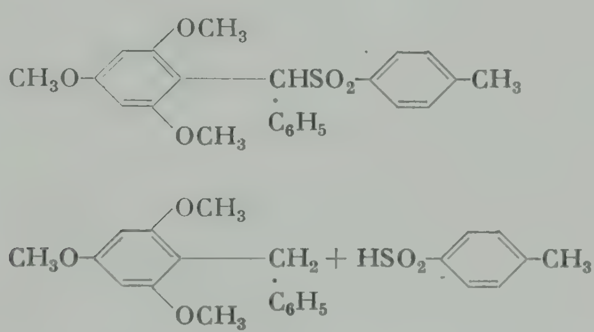
s. *9*, 876

Sulfur ↓ HC⇅S

Sodium amalgam *Na,Hg*

Reductive cleavage of sulfones $RSO_2R' \rightarrow RH + HSO_2R'$
to hydrocarbons and sulfinic acids

139.

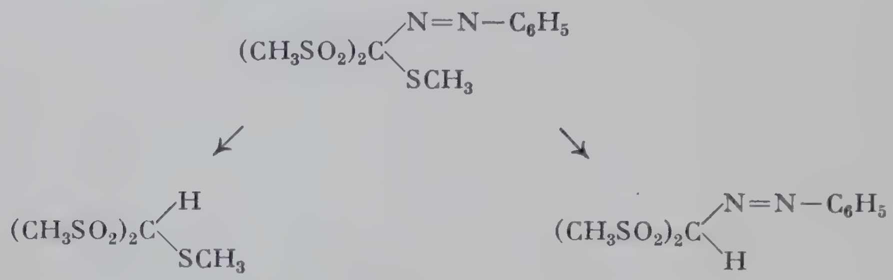


p-Tolyl 2,4,6-trimethoxydiphenylmethyl sulfone in ethanol refluxed 4 hrs. with 6%-Na,Hg → 2,4,6-trimethoxydiphenylmethane (Y: 88%) and Na-p-toluenesulfinate.—A necessary condition for this reaction seems to be that the SO_2-group is attached to at least one ar. radical. The hydrocarbon is derived from the radical of more pronounced electron-releasing character. F. e. s. R. E. Dabby, J. Kenyon, and R. F. Mason, Soc. *1952*, 4881.

Piperidine *$C_5H_{11}N$*

Cleavage of azosulfonylthioethers ←

140.



Phenylazo(methylthio)bis(methylsulfonyl)methane

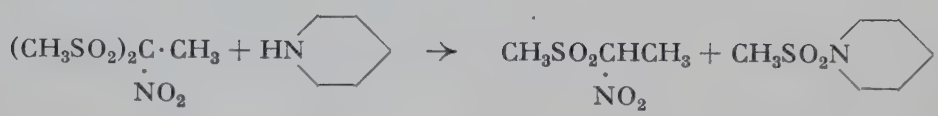
heated in HCl-alcohol-water → methylthiobis(methylsulfonyl)-methane. Y: 87%.

heated to boiling in piperidine → phenylazobis(methylsulfonyl)methane. Y: 91%.

Also removal of a methylsulfonyl group s. H. J. Backer. R. *70,* 892 (1951).

Cleavage of sulfonylnitro compounds

141.

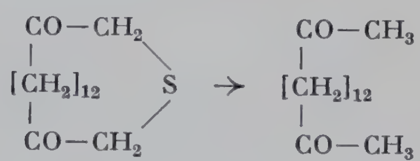


1,1-Bis(methylsulfonyl)-1-nitroethane and piperidine in dioxane warmed 1 min. at 70° → 1-methylsulfonyl-1-nitroethane (Y: 86%) and 1-methylsulfonylpiperidine (Y: 75%). H. J. Backer, R. *71,* 740 (1952).

Zinc amalgam *Zn,Hg*

Ketones from ketothioethers ←

142.



A soln. of thiacycloheptadecane-3,16-dione in acetic acid-concd. HCl refluxed several hrs. with Zn-amalgam on a steam bath, while more HCl is added each hr., until H_2S is no longer evolved, and allowed to stand overnight → 2,15-hexadecanedione. Y: 91%.—If the reaction is interrupted at the right time to prevent the diketone from further reduction, the yield is very high. F. e. s. T. Bacchetti and L. Canonica, G. *82,* 243 (1952).

Lithium aluminum hydride *$LiAlH_4$*

Methylamines from isothiocyanates $N{:}C{:}S \rightarrow NHCH_3$

143. $$C_6H_5NCS \rightarrow C_6H_5NHCH_3$$

A soln. of phenylisothiocyanate in abs. ether added dropwise during 40 min. to an ethereal soln. of $LiAlH_4$, whereby the ether starts boiling, refluxed 30 min. after the addition $\rightarrow$ crude N-methylaniline. Y: 78%. W. Ried and F. Müller, B. *85*, 470 (1952).

Sulfuric acid *H_2SO_4*

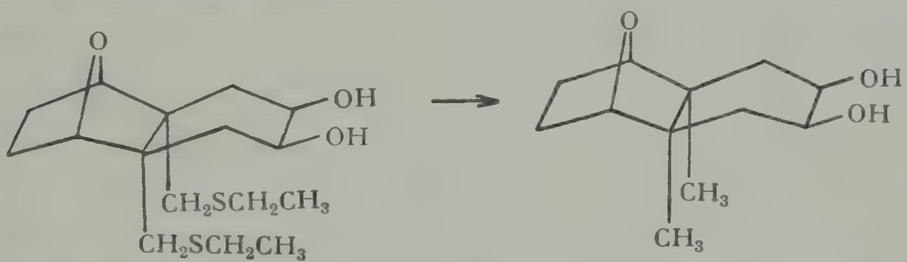
Desulfonation $SO_3H \rightarrow H$

s. *9*, 306

Nickel *Ni*

Hydrocarbons from thioethers $RSR' \rightarrow RH$

144.



A soln. of *exo*-5,8-epoxy-9,10-*cis*-di(ethylthiomethyl)-*cis*-2,3-dihydroxydecalin in 95%-ethanol stirred at reflux with Raney-Ni W 6 (s. Org. Synth. *29*, 24 (1949)) under N_2 for 1 hr. $\rightarrow$ *exo*-5,8-epoxy-9,10-*cis*-dimethyl-*cis*-2,3-dihydroxydecalin. Y: 75%. G. Stork et al., Am. Soc. *75*, 384 (1953).

Replacement of alkylthio groups by hydrogen in pyrimidines

s. *8*, 123; s. a. B. R. Baker, J. P. Joseph, and R. E. Schaub, J. Org. Chem. *19*, 631, 638 (1954)

Hydrocarbons from sulfones and thioethers ←
Stereochemistry of reductive desulfuration

145.

$$C_6H_5\cdot\overset{CH_3}{\underset{SO_2C_6H_5}{C}}\cdot CONH_2 \xrightarrow{} (+)\ C_6H_5\cdot\overset{CH_3}{\underset{H}{C}}\cdot CONH_2 \xleftarrow{} (rac.)\ C_6H_5\cdot\overset{CH_3}{\underset{SC_6H_5}{C}}\cdot CONH_2$$

The optical activity of sulfones with an asymmetric center adjacent to the S-atom is retained in reductive desulfuration; the respective thioethers, however, are completely racemized.—E:

(+)-2-Phenyl-2-benzenesulfonylpropionamide	(+)-2-Phenyl-2-phenylmercaptopropionamide

refluxed 5 hrs. with Mozingo-Raney-Ni in ethanol →

(+)-2-phenylpropionamide. Crude Y: 100%.	optically inactive 2-phenylpropionamide. Crude Y: 93%.

F. e. s. W. A. Bonner, Am. Soc. *74*, 1034 (1952).

Phenanthridines from phenanthrithiones ←

s. *9*, 574

Hydrocarbons from 1,1-disulfones $C(SO_2R)_2 \rightarrow CH_2$

s. *9*, 880

Ring opening by desulfuration

146. 

Thiophene ring opening. 5-Methoxy-2-thenoic acid and $NaHCO_3$ in water shaken with Raney-Ni (Adkins W 7) 5 hrs. at room temp., then heated 30 min. at 75° → 5-methoxyvaleric acid. Y: 82%. J. Sicé, Am. Soc. *75*, 3697 (1953).

Thiazole ring opening

s. *8*, 124; thiazolidine ring opening s. R. L. Hodgson, J. R. C. Bick, and D. J. Cram, Am. Soc. *76*, 1137 (1954)

Remaining Elements ↑ HC⇅Rem

Sodium/alcohol or potassium hydroxide/alcohol *NaOR or KOH/C_2H_5OH*

Cleavage of silanes ←

147. $(C_6H_5)_3CSi(CH_3)_3 \rightarrow (C_3H_5)_3CH$

Triphenylmethyltrimethylsilane refluxed 4 hrs. with Na-ethoxide or KOH in ethanol → triphenylmethane. Y: 97%. F. e. s. C. R. Hauser and C. R. Hance, Am. Soc. *73*, 5846 (1951).

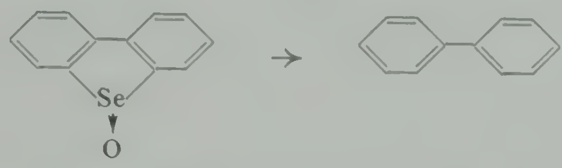
Potassium acetate *CH_3COOK*

s. *9*, 316

Nickel *Ni*

Deselenization

8.



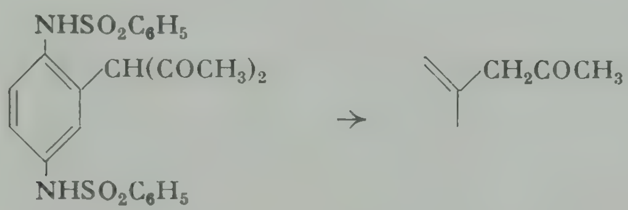
A mixture of dibenzoselenophene oxide, Raney-Ni, benzene, and ethanol refluxed 5 hrs. in an oil bath → biphenyl. Y: 72%. F. e. s. G. E. Wiseman and E. S. Gould, Am. Soc. *76*, 1706 (1954).

Carbon ↑ HC⇈C

Sodium hydroxide *NaOH*

Replacement of C-acyl by hydrogen COR → H

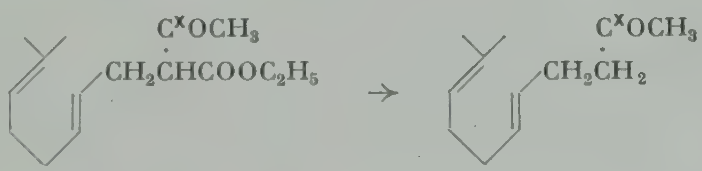
49.



3-(2,5-Dibenzenesulfonamidophenyl)-2,4-pentanedione added at 100° to aq. 2.5%-NaOH, and heating continued for 10 min. → crude 2,5-dibenzenesulfonamidophenyl-2-propanone. Y: 88%. Also carboxylic acids from β-ketocarboxylic acid esters s. R. Adams and D. C. Blomstrom, Am. Soc. *75*, 3403 (1953).

Ketones from COOR → H
β-ketocarboxylic acid esters

50.



A soln. of crude labeled ethyl geranylacetoacetate in ethanol-water containing NaOH refluxed 48 hrs. → labeled geranylacetone. Y: 90%. —The usual $Ba(OH)_2$-method gives inconsistent results. W. G. Dauben and H. L. Bradlow, Am. Soc. *74*, 5204 (1952).

Replacement of carbalkoxy groups by hydrogen at low temp.

151.

$$\begin{array}{c} C_6H_5CHNHCOCH_3 \\ \dot{C}HNO_2 \\ \dot{C}OOC_2H_5 \end{array} \rightarrow \begin{array}{c} C_6H_5CHNHCOCH_3 \\ \dot{C}H_2NO_2 \end{array}$$

Ethyl α-nitro-β-acetylamino-β-phenylpropionate (prepn. s. 841) dissolved in the cold in 10%-NaOH, and allowed to stand 68 hrs. at 0° → α-nitro-β-acetylamino-β-phenylethane. Crude Y: 88%. F. e. s. G. Stefanović, J. Bojanović, and K. Sirotanović, J. Org. Chem. *17*, 1110 (1952).

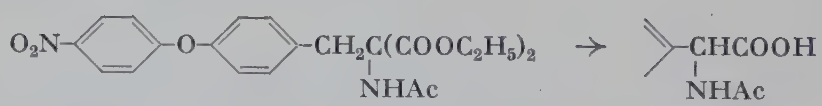
Potassium hydroxide *KOH*

Ketones from α-aminomethyleneketones $C{:}CHNR_2 \rightarrow CH_2$
Blocking of ketone α-positions
s. *9*, 769

γ-Diketones from β,γ'-diketocarboxylic acid esters $COOR \rightarrow H$
s. *9*, 892

α-Acylaminocarboxylic acids from α-acylaminomalonic acid esters

152.



A soln. of diethyl 4-(4′-nitrophenoxy)benzylacetamidomalonate and KOH in 95%-ethanol refluxed 1 hr., most of the ethanol distilled off, the residue dissolved in water, filtered, and acidified with concd. HCl → α-acetamido-β-[4-(4′-nitrophenoxy)phenyl]propionic acid. Y: 87%. P. L. Southwick, G. E. Foltz, and W. E. McIntyre, Jr., Am. Soc. *75*, 5877 (1953).

Potassium hydroxide/alcohol

Nitriles from α-cyanocarboxylic acid esters
s. *5*, 608; in ethylene glycol s. F. S. Prout, Am. Soc. *74*, 5915 (1952)

Sodium/alcohol *NaOR*

Oxo compounds from glycidic acid esters ←
s. *3*, 77; decarboxylation with dil. acetic acid instead of HCl s. M. E. Dullaghan and F. F. Nord, J. Org. Chem. *18*, 878 (1953)

Sodium amide *$NaNH_2$*

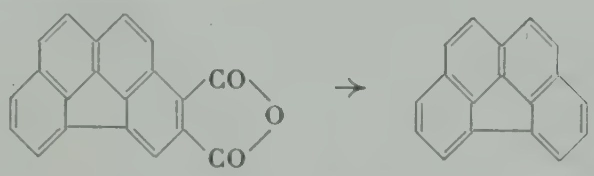
Replacement of cyano groups by hydrogen CN → H

s. 5, 81; s. a. F. F. Blicke and Eu-Phang Tsao, Am. Soc. *76*, 2203 (1954)

Calcium oxide *CaO*

Hydrocarbons from carboxylic acid anhydrides Benzo[mno]fluoranthenes ←

3.



An intimate mixture of lime and 19 mg. benzo[mno]fluoranthene-3,4-dicarboxylic acid anhydride distilled → 4 mg. benzo[mno]fluoranthene. —This is one of the first examples known of hydrocarbons having 4 ar. nuclei fused directly to a cyclopentane ring. F. e. s. N. Campbell and D. H. Reid, Soc. *1952*, 3281.

Zinc amalgam *Zn,Hg*

Hydrocarbons from β-ketocarboxylic acid esters by Clemmensen reduction ←

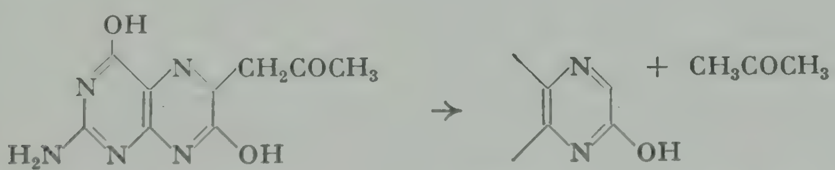
54. $$\underset{\displaystyle COOC_2H_5}{CH_3[CH_2]_{10}CHCOCH_2[CH_2]_{10}CH_3} \rightarrow CH_3[CH_2]_{10}CH_2CH_2CH_2[CH_2]_{10}CH_3$$

A mixture of ethyl 2-tridecanoyltridecanoate, abs. ethanol, and Zn,Hg satd. twice with HCl, and refluxed 20 hrs. after each introduction of HCl → pentacosane. Y: 87%. D. A. Shirley and G. A. Schmidt, Am. Soc. *73*, 5493 (1951).

Aluminum amalgam *Al,Hg*

Reductive cleavage of pyrimido[4,5-b]pyrazine side chains ←

55.

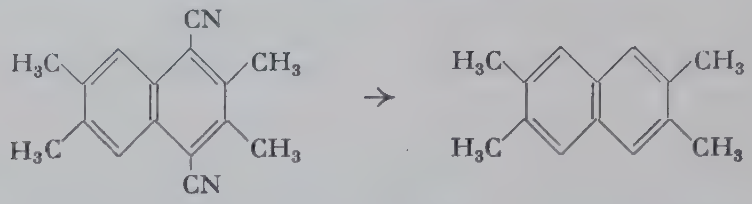


Al,Hg added to a soln. of 6-acetonylisoxanthopterin in 5%-NaOH, and heated 10 min. on a steam bath → isoxanthopterin (Y: 80%) and acetone (Y: 85% as the 2,4-dinitrophenylhydrazone). F. e. s. S. Nawa. S. Matsuura, and Y. Hirata, Am. Soc. *75*, 4450 (1953).

Polyphosphoric acid *H(PO₃H)ₓOH*

Replacement of cyano groups by hydrogen CN → H

156.



2,3,6,7-Tetramethylnaphthalene-1,4-dinitrile and polyphosphoric acid heated a short time at 200° → 2,3,6,7-tetramethylnaphthalene. Y: good. W. L. Mosby, Am. Soc. *75*, 3600 (1953).

p-Toluenesulfonic acid *TsOH*

Replacement of carbalkoxy groups by hydrogen COOR → H

tert-Butyl esters as intermediates

s. *3*, 703; *9*, 881; without solvent s. A. Treibs and K. Hintermeier, B. *87*, 1163 (1954)

Sulfuric acid *H_2SO_4*

Sulfonylacetic acid esters from sulfonylmalonic acid esters

s. *9*, 669

Replacement of cyano groups by hydrogen CN → H

s. *8*, 130; s. a. Am. Soc. *75*, 2986 (1953)

Hydrochloric acid *HCl*

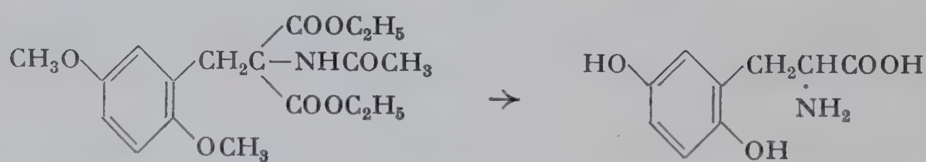
Hydroxyketones from ketolactones

s. *7*, 147; s. a. K. Winterfeld and E. Müller, A. *581*, 77 (1953)

Hydriodic acid *HI*

α-Aminocarboxylic acids from acylaminomalonic acid esters with simultaneous cleavage of ethers ←

157.



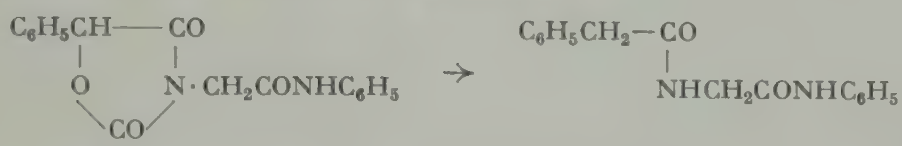
Diethyl α-acetamido-α-2,5-dimethoxybenzylmalonate refluxed 3 hrs. in a mixture of acetic acid and constant-boiling HI under a N_2-stream, with addition of small crystals of Na-hypophosphite until all iodine

color disappears when necessary → 2,5-dihydroxyphenyl-DL-alanine. Y: 65%.—Hydrolysis with HBr was not successful. F. e. s. A. T. Shulgin and E. M. Gal, Soc. *1953*, 1316.

Palladium-carbon *Pd-C*

Reductive 2,4-oxazolidione ring opening C

158.

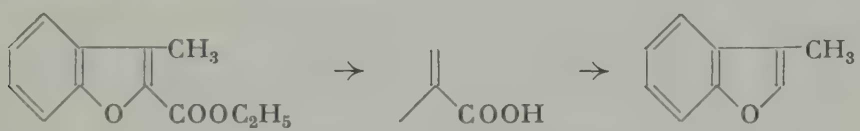


A soln. of 3-carboxanilidomethyl-5-phenyl-2,4-oxazolidione in dioxane containing 10%-Pd-on-Darco catalyst hydrogenated at atmospheric pressure until after 9 hrs. the theoretical amount of H_2 has been absorbed → phenaceturic acid anilide. Y: 91.5%. Also with Al,Hg (Y: 42%) s. J. C. Sheehan and G. D. Laubach, Am. Soc. *73*, 4752 (1951).

Via intermediates *v.i.*

Hydrolysis and decarboxylation COOR → H

159.



Ethyl 3-methylcoumarilate (prepn. s. 953) refluxed 1 hr. with aq. 10%-KOH, then acidified while hot with a slight excess of concd. HCl → 3-methylcoumarilic acid (Y: 90-95%) distilled in a Wood's metal bath, which is slowly heated to 280° → 3-methylcoumarone (Y: 84-88%). W. R. Boehme, Org. Synth. *33*, 43 (1953).

s. a. *9*, 122, 884

Elimination

Oxygen ↑ HC⇑O

Lithium aluminum hydride *$LiAlH_4$*

Aldehydes from carboxylic acids COOH → CHO

s. *9*, 112

Titanium dioxide/formic acid *TiO_2/HCOOH*

Aldehydes from carboxylic acids COOH → CHO

s. *1*, 105; negative results s. A. J. Barduhn and K. A. Kobe. Soc. *1954*, 1651

Copper chromite *$CuCr_2O_4$*

Hydrocarbons from alcohols OH → H

s. *3*, 85; s. a. J. H. Lamneck, Jr., and P. H. Wise, Am. Soc. *76*, 3475 (1954)

Hydriodic acid/acetic anhydride *$HI/(CH_3CO)_2O$*

Hydrocarbons from diols OH → H

160. $$\mathrm{Mes\underset{OH}{C}HCH_2CH_2CH_2\underset{OH}{C}HMes} \rightarrow \mathrm{Mes[CH_2]_5Mes}$$

48%-HI added dropwise to a mixture of 1,5-dimesitylpentane-1,5-diol, acetic anhydride, and glacial acetic acid, then refluxed 30 min. → 1,5-dimesitylpentane. Y: 81%.—Also reduction of glycols s. R. C. Fuson and H. P. Wallingford, Am. Soc. *75*, 5950 (1953).

Via intermediates *v.i.*

Hydrocarbons from alcohols via halides

s. *9*, 108

s. a. *1*, 108; reduction in the presence of NH_3 s. R. H. Mizzoni and P. E. Spoerri, Am. Soc. *76*, 2201 (1954)

Sulfur ↓ HC ⇑ S

Nitric acid/nitrous acid *HNO_3/HNO_2*

Replacement of sulfhydryl by hydrogen SH → H

s. *6*, 142; s. a. R. G. Jones, Am. Soc. *74*, 1085 (1952)

Carbon HC ⇑ C

Without additional reagents *w.a.r.*

Decarboxylation COOH → H

s. *9*, 159

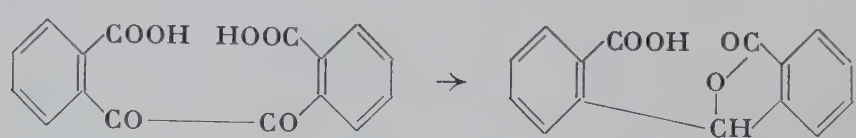
by azeotropic distillation

s. *9*, 122

Potassium hydroxide *KOH*

Phthalides ←

161.



Benzil-2,2′-dicarboxylic acid (prepn. s. 213) heated with aq. 50%-KOH at 125-130°, kept 2-5 min. at this temp., treated with water and HCl →

o-carboxyphenylphthalide. Y: 96%. C. Graebe and P. Juillard, A. *242*, 238 (1887); s. a. E. D. Bergmann and Z. Pelchowicz, Am. Soc. *75*, 4281, (1953).

Copper-nickel *Cu-Ni*

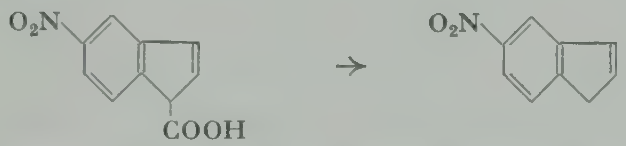
Dehydroxymethylation $CH_2OH \rightarrow H$

2. 

Tetrahydrofurfuryl alcohol allowed to react with a Cu-Ni catalyst, containing 44% Ni, at 250° using H_2 as carrier → tetrahydrofuran. Y: 88%. W. H. Bagnall, E. P. Goodings, and C. L. Wilson, Am. Soc. *73*, 4794 (1951).

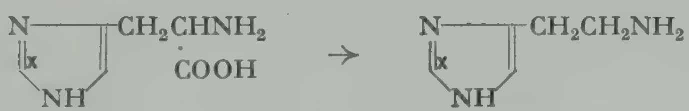
Dimethylformamide *$HCON(CH_3)_2$*

Decarboxylation $COOH \rightarrow H$

3. 

A soln. of 1 g. 5-nitro-1-indenecarboxylic acid in dimethylformamide heated on a water bath whereby CO_2-evolution starts at 45°, the temp. maintained 5 min. at 95° after the CO_2-evolution has subsided → 0.73 g. 5-nitroindene. F. e. s. O. Süs et al., A. *579*, 133 (1953).

Enzyme ←

4. 

Histidine decarboxylase from Lactobacilli added to (radioactive) L-histidine in a Warburg flask, and incubated 65 min. at 30° until CO_2-evolution is complete → (radioactive) histamine. Y: 65% as the dipicrate. R. W. Schayer, Am. Soc. *74*, 2440 (1952).

Nickel-copper s. Copper-nickel *Ni-Cu*

Nickel-silica *Ni-SiO_2*

Dehydroxymethylation $CH_2OH \rightarrow H$

s. *6*, 145; s. a. H. Pines, H. G. Rodenberg, and V. N. Ipatieff, Am. Soc. *75*, 6065 (1953); *76*, 771 (1954)

Via intermediates *v.i.*

Aldehydes from α-ketocarboxylic acids $COCOOH \rightarrow CHO$

s. *2*, 689; s. a. R. Schwarz and K. Capek, M. *83*, 883 (1952)

Formation of O—O Bond

Uptake

Addition to Oxygen and Carbon OO ⇓ OC

Sodium hydroxide *NaOH*

Acyl peroxides from carboxylic acid anhydrides $\cdot CO\cdot O\cdot OC\cdot \rightarrow \cdot CO\cdot OO\cdot OC\cdot$

165. $C_2H_5\cdot CO\cdot O\cdot OC\cdot C_2H_5 \rightarrow C_2H_5\cdot CO\cdot OO\cdot OC\cdot C_2H_5$

Aq. NaOH added dropwise during 2 hrs. below 0° to a mixture of propionic anhydride and 30%-H_2O_2, stirring continued for 1 hr., then extracted with ether → propionyl peroxide. Y: 90-95%; containing 95-98% peroxide. S. Goldschmidt, W. Leicher, and H. Haas, A. *577*, 153 (1952).

Exchange

Sulfur ↑ OO⇅S

Potassium hydroxide *KOH*

Hydroperoxides from methylsulfonates $\cdot OSO_2CH_3 \rightarrow \cdot OOH$

166. $(CH_3)_2CH{-}CH_2CH_2OSO_2CH_3 \rightarrow (CH_3)_2CH{-}CH_2CH_2OOH$

A one-phase reaction mixture prepared by adding aq. 50%-KOH to a chilled soln. of isoamyl methanesulfonate, 30%-H_2O_2, methanol, and water kept 20 hrs. at room temp. in a water bath → isoamyl hydroperoxide. Y: 52.0%.—This method makes potentially available a wide variety of alkyl hydroperoxides previously inaccessible. F. e., with lower yields, s. H. R. Williams and H. S. Mosher, Am. Soc. *76*, 2987, 2984 (1954).

Formation of O—N Bond

Uptake

Addition to Nitrogen ON⇓N

Peracetic acid *CH_3COO_2H*

N-Oxides N→O

s. 8, 136; 2-aminopyridine 1-oxides s. R. Adams and S. Miyano, Am. Soc. *76*, 2785 (1954)

Trifluoroperacetic acid *CF_3COO_2H*

N-Nitramines from N-nitrosamines $N \cdot NO \rightarrow N \cdot NO_2$

s. *9*, 169

Perphthalic acid

Azoxy compounds from hydrazones and reverse reaction $CH{:}N \cdot NHR \underset{\leftarrow}{\rightarrow} CH_2\overset{}{N}(\rightarrow O){:}NR$

167. $$C_6H_5CH{=}N \cdot NHC_6H_5 \rightleftarrows C_6H_5CH_2\underset{\downarrow \atop O}{N}{=}NC_6H_5$$

Perphthalic acid in ether added to benzaldehyde phenylhydrazone, and the product isolated after 2 days → benzylazoxybenzene (Y: 96%), 0.45 g. in dry ether refluxed 8 hrs. with $LiAlH_4$ → 0.35 g. benzaldehyde phenylhydrazone. F. azoxy compounds s. B. M. Lynch and K. H. Pausacker, Soc. *1953*, 2517.

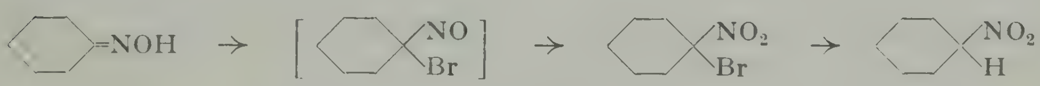
Nitrogen dioxide *NO_2*

Hydroxyhydrazines from hydrazyl radicals $N \cdot N(OH)$

s. *9*, 988

Nitric acid *HNO_3*

Aliphatic nitro compounds from oximes via 1,1-bromonitroso- and 1,1-bromonitro compounds $NO \rightarrow NO_2$

168.


An aq. soln. of cyclohexanone oxime and $NaHCO_3$ added as rapidly as possible during ca. 15 min. at about 10° to a vigorously stirred aq. suspension of N-bromosuccinimide, stirring continued for 15 min., extracted with petroleum ether, concentrated, and shaken with HNO_3 (d. 1.42) until the blue color disappears → 1-bromo-1-nitrocyclohexane (Y: 63%) added dropwise to $NaBH_4$ in aq. 75%-methanol—if necessary with external heating to start the reaction—, and the remainder added as rapidly as possible when the solvent is at reflux temp. → nitrocyclohexane (Y: 80%). F. e. s. D. C. Iffland and G. X. Criner, Am. Soc. *75*, 4047 (1953); *76*, 4083 (1954).

Hydrogen peroxide *H_2O_2*

N-Oxides $N \rightarrow O$

s. *9*, 243

Exchange

Hydrogen ↑ ON⇅H

Potassium salt *K^+*

O-Azo compounds ·ON:NR
s. *9*, 419

Trifluoroperacetic acid *CF_3COO_2H*

Oxidations with trifluoroperacetic acid ←
Nitro compounds from amines
N-Nitramines from N-nitrosamines

169. 

$(C_4H_9)_2N \cdot NO \rightarrow (C_4H_9)_2N \cdot NO_2$

90%-H_2O_2 added at 20° to trifluoroacetic acid, then p-aminobenzonitrile added in one portion, the temp. allowed to rise to 50° and kept there by intermittent cooling for 1 hr. → p-nitrobenzonitrile. Y: 98%. —Similarly: Dibutylnitrosamine → dibutylnitramine. Y: 77%. W. D. Emmons and A. F. Ferris, Am. Soc. *75*, 4623 (1953); *76*, 3468, 3470 (1954).

Hydrogen peroxide/sulfuric acid *H_2O_2/H_2SO_4*

Nitro compounds from amines $NH_2 \rightarrow NO_2$
s. *7*, 160; s. a. E. V. Brown, Am. Soc. *76*, 3167 (1954)

Oxygen ↑ ON⇅O

Acetic anhydride *$(CH_3CO)_2O$*

Nitric acid esters ONO_2
s. *3*, 101; of glycosides s. D. M. Shepherd, Soc. *1953*, 3635

Elimination

Hydrogen ↑ ON⇑H

Phenyl iodosoacetate *$C_6H_5I(OAc)_2$*

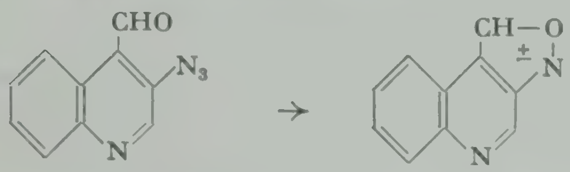
Benzofurazan oxides from o-nitramines
s. *9*, 385

Nitrogen ↑ **ON ⇑ N**

Without additional reagents *w.a.r*

Isoxazole ring from o-azidoöxo compounds ○

70.



0.6 g. 3-azidoquinoline-4-aldehyde (prepn. s. 382) and dioxane refluxed 4 hrs. → 0.35 g. quinolino(3′,4′:3,4)isoxazole. D. W. Ockenden and K. Schofield. Soc. *1953*, 1915; s. a. P. A. S. Smith et al., Am. Soc. *75*, 6335 (1953).

Formation of O—Hal Bond

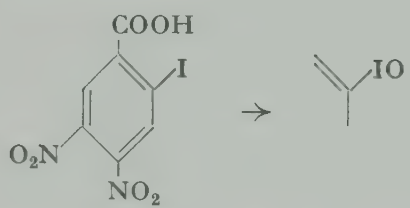
Uptake

Addition to Halogen **OHal ⇓ Hal**

Nitric acid *HNO_3*

Iodoso compounds from iodides I → IO

71.



4,5-Dinitro-2-iodobenzoic acid dissolved in HNO_3 (d. 1.52) and heated 3 min. on a steam bath → 4,5-dinitro-2-iodosobenzoic acid. Y: 92%. H. Goldstein and R. Jaunin, Helv. *34*, 2222 (1951).

Hydrogen peroxide *H_2O_2*

Iodosoacetates $I(OAc)_2$

72. $C_6H_5I \rightarrow C_6H_5I(OCOCH_3)_2$

30%-H_2O_2 and acetic anhydride stirred together for 4 hrs. at 40°, 50 g. iodobenzene added, and allowed to stand overnight → 52 g. phenyl iodosoacetate. F. e. by a second method s. K. H. Pausacker, Soc. *1953*, 107.

Formation of O—S Bond

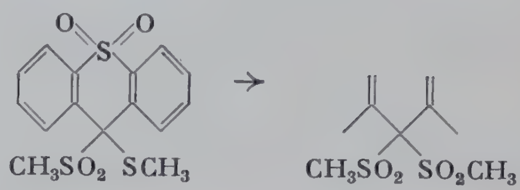
Uptake

Addition to Sulfur **OS ⇓ S**

Perbenzoic acid *$C_6H_5COO_2H$*

Sulfones from thioethers $>S \rightarrow >SO_2$

173.



10-(Methylthio)-10-(methylsulfonyl)thiaxanthene 5,5-dioxide allowed to react with 4 equivalents perbenzoic acid in chloroform at room temp. for 20 hrs. → 10,10-bis(methylsulfonyl)thiaxanthene 5,5-dioxide. Y: 81%. F. e. s. H. Kloosterziel, W. van der Veen, and H. J. Backer, R. *71*, 1231 (1952).

1,1-Disulfones from mercaptals

s. *9*, 342

Hydrogen peroxide *H_2O_2*

Sulfoxides and sulfones from thioethers $R_2S \rightarrow R_2SO$; $R_2S \rightarrow R_2SO_2$

s. *1*, 116; *5*, 101; s. a. D. Jerchel, L. Dippelhofer, and D. Renner, B. *87*, 947 (1954)

Potassium permanganate *$KMnO_4$*

s. *6*, 148; cyclic sulfones s. A. R. Surrey and R. A. Cutler, Am. Soc. *76*, 578 (1954)

Ruthenium tetroxide *RuO_4*

174. $C_6H_5CH_2SCH_3 \rightarrow C_6H_5CH_2SO_2CH_3$

Oxydations with ruthenium tetroxide. Methyl benzyl sulfide allowed to react with RuO_4 in CCl_4 → methyl benzyl sulfone. Y: 58%. F. e. s. C. Djerassi and R. R. Engle, Am. Soc. *75*, 3838 (1953).

Exchange

Hydrogen ↓ OS⇅H

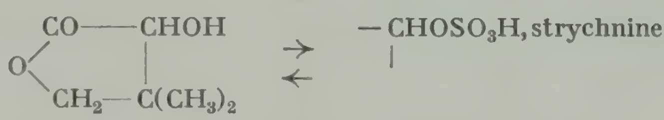
Without additional reagents *w.a.r.*

Sulfuric acid monoesters OSO_3H

175. $H_2NCH_2CH_2CH_2OH + H_2SO_4 \rightarrow H_2NCH_2CH_2CH_2OSO_3H$

An aq. soln. of γ-aminopropanol added dropwise with cooling to H_2SO_4-water, then distilled under slightly reduced pressure until the temp. of the reaction mixture reaches 190° → crude γ-aminopropylsulfuric acid. Y: 90%. H. W. Heine et al., Am. Soc. 75, 2505 (1953).

Resolution of reacemates via salts
Optically active alcohols
via sulfuric acid ester salts

176. 

Chlorosulfonic acid added with stirring and ice-cooling portionwise to a soln. of DL-pantolactone in chloroform, stirring continued 3 hrs. with ice-cooling and 12 hrs. at room temp., extracted with water, small portions of $NaHCO_3$ added with stirring, adjusted to pH 6 with 2 *N* NaOH, stirring continued and treated with a warm aq. soln. of strychnine hydrochloride, then allowed to stand 1-2 days at room temp. → strychnine D(–)-pantolactone sulfate (Y: 70-80%) dissolved in aq. H_2SO_4 by heating and swirling, refluxing continued for 5 hrs. → crude D(–)-pantolactone (Y: ca. 95%). F. Bergel et al., B. 85, 711 (1952).

Thionyl chloride $SOCl_2$

Chlorosulfinates OSOCl

s. 4, 144; s. a. G. Berti, Am. Soc. 76, 1213 (1954)

Oxygen ↓ OS⇅O

Methoxyacetylene $HC{:}C{\cdot}OCH_3$

Sulfonic acid anhydrides from sulfonic acids $2\ RSO_3H \rightarrow (RSO_2)_2O$

s. 9, 261

Carbodiimides *RN=C=NR*

Reactions with carbodiimides
Sulfonic acid anhydrides from sulfonic acids

177. $$2\ CH_3SO_3H + C\begin{matrix} \diagup NC_6H_4CH_3\text{-p} \\ \diagdown NC_6H_4CH_3\text{-p} \end{matrix} \rightarrow CH_3SO_2 \cdot OSO_2CH_3 + OC\begin{matrix} \diagup NHC_6H_4CH_3\text{-p} \\ \diagdown NHC_6H_4CH_3\text{-p} \end{matrix}$$

A soln. of di-p-tolyl carbodiimide in anhydrous benzene added quickly to methanesulfonic acid, and the mixture agitated vigorously for 1 hr. → methanesulfonic anhydride (startg. m. f. 391). Y: ca. 92%. F. e. s. H. G. Khorana, Can. J. Chem. *31*, 585 (1953); phosphoric acid derivatives s. Am. Soc. *76*, 3517, 3522 (1954).

Phosphorus pentoxide *P_2O_5*

178. $$2\ C_6H_5SO_3H \rightarrow (C_6H_5SO_2)_2O$$

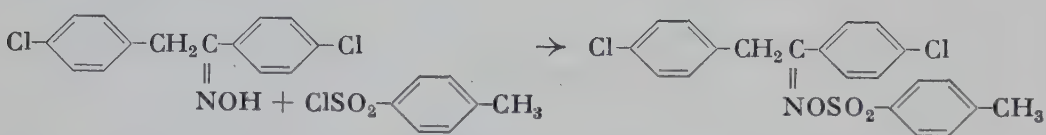
One-half of a mixture of P_2O_5, kieselguhr, and asbestos mixed with benzenesulfonic acid sesquihydrate, the hot mixture allowed to stand 0.5 hr., then the remainder of the mixture mixed in as well as possible at 100° during 2 hrs., and heating continued for 5 hrs. with occasional mixing → benzenesulfonic acid anhydride (startg. m. f. 669, 671). Y: 50-60%.—Admixture of kieselguhr and asbestos facilitates subsequent extraction. F. e. s. L. Field, Am. Soc. *74*, 394 (1952).

Halogen ↓ OS ⇅ Hal

Potassium hydroxide *KOH*

Oxime sulfonates C:NOSO$_2$R

179.



p-Toluenesulfonyl chloride added portionwise at 0-7° during 10 min. to a vigorously stirred soln. of p,p′-dichlorodesoxybenzoinoxime and KOH in acetone-water, and stirring continued 25 min. at the same temp. → p,p′-dichlorodesoxybenzoinoxime tosylate (startg. m. f. 242). Y: 72%. F. e. s. M. J. Hatch and D. J. Cram, Am. Soc. *75*, 38 (1953).

Pyridine *C_5H_5N*

p-Toluenesulfonic acid esters as intermediates OSO$_2$R

s. *9*, 623

Partial O-tosylation

s. *9*, 825; s. a. W. F. Johns, R. M. Lukes, and L. H. Sarett, Am. Soc. *76*, 5026 (1954)

γ-Collidine ←

Sulfonic acid esters
from sulfonic acid chlorides and alcohols

0. $CH_2{=}CHCH_2OH + ClSO_2C_6H_5 \rightarrow CH_2{=}CHCH_2OSO_2C_6H_5$

Benzenesulfonyl chloride added dropwise at −5 to 0° to a mixture of allyl alcohol and γ-collidine, and stirring of the cooled mixture continued for 1 hr. → allyl benzenesulfonate. Y: 66%.—A better yield is obtained with γ-collidine than with pyridine. Apparently the formation of quaternary ammonium salts is minimized by the use of a more sterically hindered base. C. G. Bergstrom and S. Siegel, Am. Soc. *74*, 254 (1952).

Mercuric oxide *HgO*

Sulfonic acid anhydrides $2\,RSO_2Cl \rightarrow RSO_2\cdot O\cdot O_2SR$
from sulfonic acid chlorides

81. $2\,CH_3SO_2Cl \rightarrow (CH_3SO_2)_2O$

A mixture of methanesulfonyl chloride, yellow HgO, and *sym*-tetrachloroethane refluxed 1.5 hrs. with stirring at 146° under anhydrous conditions until all odor of sulfonyl chloride has disappeared, then for 10 min. more → methanesulfonic anhydride. Y: 67-82%. F. e. s. L. Field and P. H. Settlage, Am. Soc. *76*, 1222 (1954).

Formation of O—Rem Bond

Uptake

Addition to Hydrogen and Oxygen ORem ⇓ HO

Without additional reagents *w.a.r.*

Phosphorylation with subsequent formation ←
of aldehydes from amines

s. 8, 250; s. a. E. A. Peterson, H. A. Sober, and A. Meister, Biochem. Prep. *3*, 29, 34 (1953); Am. Soc. *76*, 169 (1954)

Addition to Hydrogen and Remaining Elements ORem ⇓ HRem

Via intermediates *v.i.*

Phosphinic acids from phosphine oxides $R_2P(O)H \rightarrow R_2P(O)OH$

82. $(n\text{-}C_8H_{17})_2P(O)H \rightarrow [(n\text{-}C_8H_{17})_2P(O)Cl] \rightarrow (n\text{-}C_8H_{17})_2P(O)OH$

Cl_2-gas bubbled slowly into a soln. of di-n-octylphosphine oxide (prepn. s. 724) in CCl_4 maintained at 0-9° until the color of Cl_2 persists, the

soln. of the phosphinyl chloride then treated with an aq. soln. of K-carbonate, followed by acidification with 15%-H_2SO_4 soln. → di-n-octylphosphinic acid. Y: 86.6%. Also direct oxidation with H_2O_2 and f. e. by this method s. R. H. Williams and L. A. Hamilton, Am. Soc. *74*, 5418 (1952).

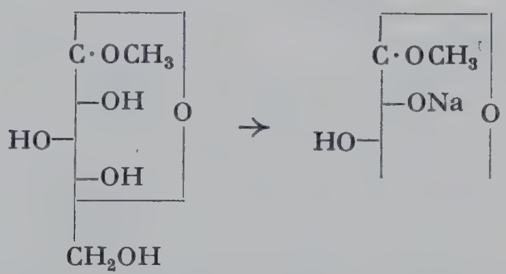
Exchange

Hydrogen ↑ ORem ⇅ H

Without additional reagents *w.a.r.*

Sodio derivatives of carbohydrates OH → ONa
Differential reactivity of hydroxyl groups

183.



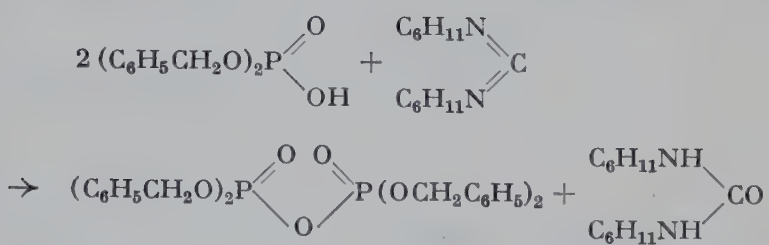
A hot soln. of 1.25 molar equivalents of powdered anhydrous NaOH in 1-butanol added with stirring to a warm soln. of dry methyl α-D-glucopyranoside in 1-butanol, and the water formed removed by azeotropic distillation with 1-butanol → crude methyl monosodio-α-D-glucopyranoside. Y: 96%. M. L. Wolfrom and M. A. El-Taraboulsi, Am. Soc. *75*, 5350 (1953).

Oxygen ↑ ORem ⇅ O

Carbodiimides *RN:C:NR*

Pyrophosphoric acid esters $(RO)_2PO\cdot O\cdot OP(OR)_2$

184.



Pyridine followed by dicyclohexylcarbodiimide added to a soln. of dibenzyl hydrogen phosphate in benzene, the dicyclohexylurea formed filtered off after 15 min., and the filtrate evaporated → tetrabenzyl pyrophosphate. Y: 93%. F. e., without pyridine, also in the presence of water, and pyrophosphoric acid diesters from phosphoric acid monoesters, s. H. G. Khorana and A. R. Todd, Soc. *1953*, 2257.

Halogen ↓ ORem ⇅ Hal

Sodium hydroxide *NaOH*

Germanecarboxylic acid germyl esters $R_3GeCOOGeR_3$

s. *9*, 195

Potassium hydroxide/alcohol *KOH*

Germanols from halogenogermanes GeHal → GeOH

from chlorogermanes s. *5*, 105; from bromogermanes s. A. G. Brook and H. Gilman, Am. Soc. *76*, 77 (1954)

Ammonia *NH_3*

Titanic acid esters $Ti(OR)_4$

185. $$TiCl_4 + 4\ n\text{-}C_4H_9OH \rightarrow Ti(OC_4H_9\text{-}n)_4$$

110 g. $TiCl_4$ and n-butanol in benzene treated with NH_3 → 115 g. titanium tetra-n-butoxide. F. e. s. D. C. Bradley, D. C. Hancock, and W. Wardlaw, Soc. *1952*, 2773.

Triethylamine *$(C_2H_5)_3N$*

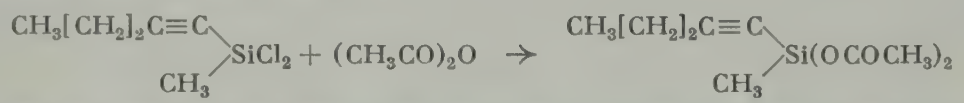
Peptide synthesis with chlorophosphites ←

s. *9*, 475

Triethanolamine *$(HOCH_2CH_2)_3N$*

Acoxy- from halogeno-silanes ←

186.



1-Pentynylmethyldichlorosilane refluxed 1.5 hrs. with acetic anhydride in the presence of a small amount of triethanolamine → 1-pentynylmethyldiacetoxysilane. Y: 85%. F. e. s. K. C. Frisch and R. B. Young. Am. Soc. *74*, 4853 (1952).

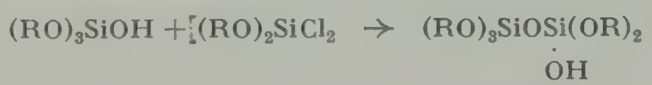
Pyridine *C_5H_5N*

Reaction of boron trichloride with alcohols ←
Boric acid esters

s. *8*, 152; s. a. Soc. *1953*, 667

Siloxanols from halogenosilanes ←

187.



Tris-(1.3-dimethylbutoxy)silanol added dropwise to a cold stirred mixture of dis-(1.3-dimethylbutoxy)dichlorosilane and dry pyridine. then water added rapidly, and stirred 1 hr. → pentakis-(1,3-dimethylbutoxy)disiloxanol. Y: 86%. F. e. s. C. R. Morgan, W. F. Olds, and A. L. Rafferty, Am. Soc. *73*, 5193 (1951).

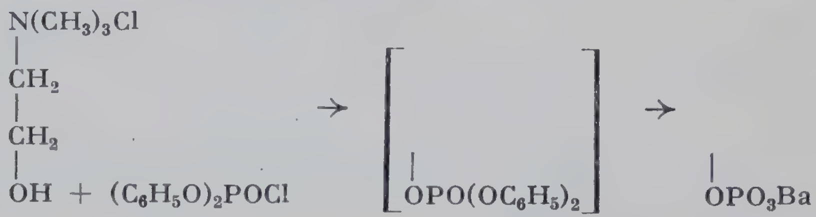
Mixed phosphites $(RO)_2P(OR')$

188. $(C_6H_5O)_2PCl + HOC_6H_{11} \rightarrow (C_6H_5O)_2POC_6H_{11}$

A mixture of cyclohexanol, pyridine, and ether added dropwise during 2.5 hrs. to an ice-cooled, well-stirred soln. of diphenyl chlorophosphite and pyridine in ether, then allowed to warm to room temp. overnight with stirring → cyclohexyl diphenyl phosphite. Y: 88%. J. P. Forsman and D. Lipkin, Am. Soc. *75*, 3145 (1953).

Phosphorylation of hydroxy compounds $OH \rightarrow OPO_3^{--}$

189.



A mixture of anhydrous choline chloride, diphenylchlorophosphate, glass beads, and dry pyridine stirred vigorously at room temp. for 2 days, dissolved in water, filtered, evaporated in vacuo at a bath temp. not higher than 50°, the residue consisting of diphenylphosphorylcholine chloride and pyridine hydrochloride, dissolved in water, to the soln. added $Ba(OH)_2$, a little octyl alcohol, and a few boiling chips, then refluxed for a total of 1.25 hrs. after boiling commences → Ba salt of phosphorylcholine chloride. Y: 39-63%. E. Baer, Biochem. Prep. *2*, 96 (1952).

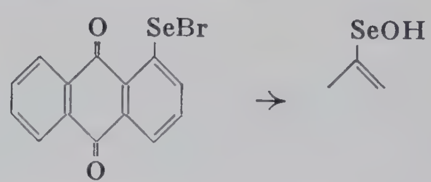
Hydrogenolysis of phosphoric acid esters

s. *6*, 158; s. a. J. H. van der Neut, J. H. Uhlenbroek, and P. E. Verkade, R. *72*, 365 (1953); C. E. Ballou and H. O. L. Fischer, Am. Soc. *76*, 3188 (1954)

Silver oxide *Ag_2O*

Selenenic acids from selenylbromides $SeBr \rightarrow SeOH$

190.

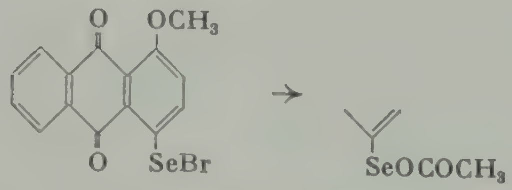


1.83 g. 1-anthraquinoneselenenyl bromide refluxed 2 hrs. with freshly prepared moist Ag_2O in dioxane, the hot mixture filtered, cooled, stirred and treated with a large amount of water → 0.9 g. crude 1-anthraquinoneselenenic acid. W. Jenny, Helv. *35*, 1591 (1952); via selenenyl acetates s. Helv. *35*, 1429.

Silver acetate *CH_3COOAg*

Selenyl acetates from selenyl halides SeHal → SeOAc

1.



1.2 g. 1-methoxyanthraquinone-4-selenenyl bromide and Ag-acetate refluxed 2 hrs. in glacial acetic acid in an oil bath → 1.03 g. 1-methoxyanthraquinone-4-selenenyl acetate. W. Jenny, Helv. *35*, 1429 (1952).

Methyl Cellosolve *$HOCH_2CH_2OCH_3$*

Silanols from halogenosilanes SiHal → SiOH

2. $(1\text{-}C_{10}H_7)_3SiCl \rightarrow (1\text{-}C_{10}H_7)_3SiOH$

Tri-1-naphthylchlorosilane in Methyl Cellosolve containing water refluxed 30 min. → tri-1-naphthylsilanol. Y: ca. 100%. H. Gilman and C. G. Brannen, Am. Soc. *73*, 4640 (1951).

Phosphorus oxychloride *$POCl_3$*

Phosphoric acid esters $(RO)_3PO$

s. *1*, 127; polyfluoro compounds s. L. C. Krogh, T. S. Reid, and H. A. Brown, J. Org. Chem. *19*, 1124 (1954)

Sulfur ↓ ORem ⇅ S

Without additional reagents *w.a.r.*

Dithiophosphoric acid esters from orthoformic acid esters ←

3. $P_2S_5 + 3\,HC(OC_2H_5)_3 \rightarrow 2\,(C_2H_5)_3PO_2S_2 + 2\,HCOOC_2H_5 + HCSOC_2H_5$

A mixture of P_2S_5 and ethyl orthoformate heated 15 min. at 95°, the heat source removed when the exothermic reaction sets in, heating resumed after 15 min., and the temp. raised to 150° over the next 30 min. as distillation progresses → crude triethyl dithiophosphate. Y: 92.5%. F. similar reactions s. K. C. Brannock, Am. Soc. *73*, 4953 (1951).

Carbon ↑ ORem ⇅ C

Without additional reagents *w.a.r.*

Cleavage of mixed ethers ←
Dichloroboric acid esters

194. $$C_2H_5OC_8H_{17} + BCl_3 \rightarrow C_2H_5OBCl_2 + ClC_8H_{17}$$

Ethyl n-octyl ether added to BCl_3 at $-10°$ → ethyl dichloroboronite (Y: 89%) and n-octyl chloride (Y: 80%). F. e., and different direction of the cleavage with HI, s. W. Gerrard and M. F. Lappert, Soc. *1952*, 1486.

Germanecarboxylic acid germyl esters $R_3GeCOOGeR_3$

195. $$2\,(C_6H_5)_3GeCOOH \searrow \qquad (C_6H_5)_3GeCOOH + BrGe(C_6H_5)_3 \swarrow$$
$$(C_6H_5)_3GeCOOGe(C_6H_5)_3$$

Triphenylgermanecarboxylic acid (prepn. s. 728)

slowly heated to 190°, then ca. 5 min. at 190-210° until gas evolution virtually ceases →

treated with aq. NaOH, gently warmed to effect soln., the water removed under reduced pressure, benzene and triphenylbromogermane added, and refluxed 2 hrs. →

Y: 86%. triphenylgermyl triphenylgermanecarboxylate. Y: 81%. A. G. Brook and H. Gilman, Am. Soc. *76*, 77 (1954).

Potassium hydroxide *KOH*

Phosphine oxides from phosphonium salts ←

196. $$(p\text{-}CH_3C_6H_4)_3(CH_3)P^+\ I^- \rightarrow (p\text{-}CH_3C_6H_4)_2(CH_3)P{=}O$$

40%-KOH added to an aq. suspension of methyltri-p-tolylphosphonium iodide, and distilled until evolution of toluene is complete → methyldi-p-tolylphosphine oxide (startg. m. f. 255). Y: 80%. F. e. s. P. W. Morgan and B. C. Herr, Am. Soc. *74*, 4526 (1952).

Sulfuric acid H_2SO_4

Siloxanes from methylsilanes ←

s. *7*, 179; s. a. Am. Soc. *75*, 2932 (1953)

Hydrochloric acid *HCl*

Diboroxides $>B\cdot O\cdot B<$

197. $$2\,[(C_6H_5)_4B]\,Na \rightarrow (C_6H_5)_2B\cdot O\cdot B(C_6H_5)_2 + 4\,C_6H_6$$

Na-tetraphenylborate shaken ca. 7 hrs. with aq. HCl until dissolved → tetraphenyldiboroxide. Y: 76%. R. Neu, B. *87*, 802 (1954).

Formation of O—C Bond

Uptake

Addition to Hydrogen and Carbon OC ⇓ HC

Electric discharge ←

Phenols from hydrocarbons H → OH

8. Benzene vapor (2-3 mm. Hg) allowed to react with O_2 (4-8 mm. Hg), which has been passed through a discharge tube at 3000-4000 V → phenol. Y: 10-13% per pass. The only heating needed is for vaporizing the benzene. Ju Chin Chu, H. C. Ai, and D. F. Othmer. Ind. Eng. Chem. *45*, 1266 (1953).

Fungi ←

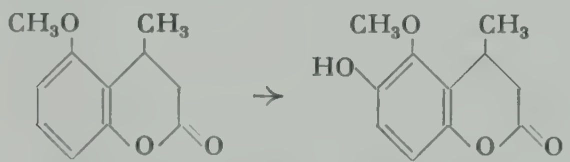
Alcohols from hydrocarbons
11-Hydroxysteroids
Bioöxygenation

s. *7*, 181; s. a. Am. Soc. *75*, 421 (1953) and other papers of this series; also O. Mancera et al., Am. Soc. *74*, 3711 (1952); J. Fried et al., Am. Soc. *74*, 3962 (1952); C. Meystre, E. Vischer, and A. Wettstein, Helv. *37*, 1548 (1954)

Persulfate $S_2O_8^{--}$

Replacement of hydrogen by hydroxyl
Elbs reaction

99.



with heterocyclics. K-persulfate added gradually with stirring during 3 hrs. below 10° to a soln. of 4.7 g. 5-methoxy-4-methylcoumarin in aq. NaOH, stirring continued for 0.5 hr., allowed to stand overnight, the next day just acidified, and extracted with ether → 2.3 g. 5-methoxy-6-hydroxy-4-methylcoumarin (startg. m. f. 29). F. e. s. V. J. Dalvi, R. B. Desai, and S. Sethna, J Indian Chem. Soc. *28*, 366 (1951); s. a. K. Aghoramurthi and T. R. Seshadri, Soc. *1954*, 3065.

Selenium dioxide SeO_2

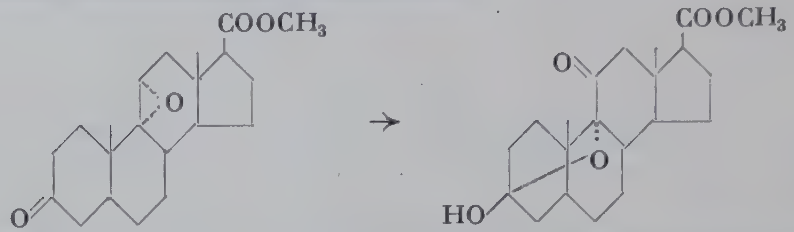
1,2,3-Hydroxydiketones from ketones ←

s. *9*, 230

Chromic acid *CrO_3*

Ketolactols from ketoöxido compounds ←

200.



A soln. of methyl 3-keto-9α-11α-oxidoetiocholanate in acetic acid treated with water and CrO_3 at room temp. for 17 hrs. → methyl 3β-hydroxy-3α,9α-oxido-11-ketoetiocholanate. Y: 70.5%. H. Heymann and L. F. Fieser, Am. Soc. *74*, 5938 (1952).

Potassium manganate and permanganate *K_2MnO_4 and $KMnO_4$*

Tert. hydroxycarboxylic acids from carboxylic acids H → OH

201. $(C_6H_5)(CH_3)CHCOOH \rightarrow (C_6H_5)(CH_3)C(OH)COOH$

An aq. soln. of K-permanganate and KOH added dropwise at ca. 40° during ca. 20 min. to α-phenylpropionic acid in concd. aq. KOH, the resulting green soln. cooled in ice, and shaken with SO_2 until colorless → α-phenyllactic acid. Y: 90%. (Soc. *1953*, 2129.)—Optically active acids are completely racemized by this procedure, but retain their optical activity by oxidation with K-manganate in dil. alkalin soln. (Soc. *1953*, 3580). The most satisfactory method of preparing tert. γ-hydroxycarboxylic acids is by a combination of the two procedures. whereby by suitable adjustment of the alkali concentration the 2 stages in reduction, $MnO_4' \rightarrow MnO_4'' \rightarrow MnO_2$, are consecutive and not simultaneous (Soc. *1953*, 2129). F. e. with both procedures and their combination s. J. Kenyon and M. C. R. Symons, Soc. *1953*, 2129, 3580.

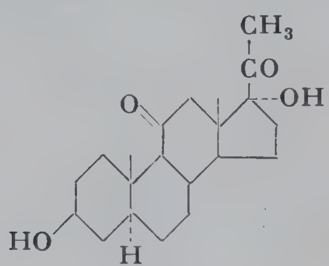
Potassium permanganate *$KMnO_4$*

Ketocarboxylic acids from hydroxyaldehydes ←
s. *9*, 364

Via intermediates *v.i.*

α-Hydroxyketones from ketones via enolesters and 1-acoxy-1,2-oxido compounds H → OH
17α-Hydroxy-20-ketosteroids

202.

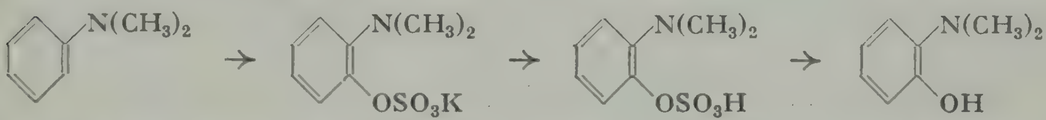


3β-Acetoxyallopregnane-11,20-dione in *carbon tetrachloride* treated at room temp. with a little aq. 50%-$HClO_4$ in acetic anhydride, kept 1.5 hrs. at room temp., the crude enolester taken up in chloroform, treated with ethereal monoperphthalic acid, allowed to stand 3 hrs. at room temp., the crude product treated with hot methanolic 0.8 *N* KOH, with rapid swirling and further heating until a crystalline material separates → 3β,17α-dihydroxyallopregnane-11,20-dione. Y: 92%. D. H. R. Barton et al., Soc. *1954*, 747; use of commercial peracetic acid and Na-acetate instead of monoperphthalic acid cf. E. P. Oliveto and E. B. Hershberg, Am. Soc. *76*, 5167 (1954); f. formulas cf. Synth. Meth. *7*, 184.

o-Hydroxylation

s. *6*, 162; s. a. Soc. *1954*, 1134

o-Aminophenols from ar. amines via o-aminosulfuric acid esters

3. 

A satd. aq. soln. of K-persulfate added with stirring during 8 hrs. to dimethylaniline and KOH in acetone-water, and allowed to stand overnight → o-dimethylaminophenyl-K-sulfate (Y: 40%) treated with aq. HCl → o-dimethylaminophenyl hydrogen sulfate (Y: 82%) heated 1 hr. at 100° with concd. HCl → o-dimethylaminophenol (Y: 83%). F. e. s. E. Boyland, D. Manson, and P. Sims, Soc. *1953*, 3623.

Addition to Oxygen — OC ⇓ OO

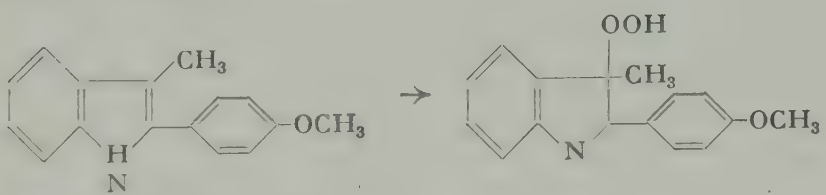
Without additional reagents — *w.a.r.*

Hydroperoxides from hydrocarbons — H → OOH

s. *1*, 132; s. a. H. B. Knight and D. Swern, Org. Synth. *34*, 90 (1954)

Platinum oxide — *PtO_2*

N-Heterocyclic hydroperoxides by catalytic oxidation ←

04. 

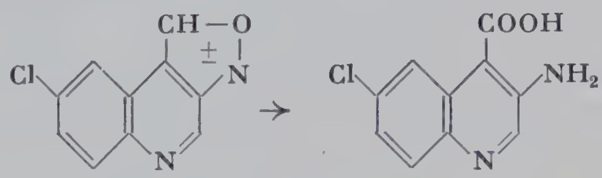
A soln. of 2-(p-methoxyphenyl)skatole in ethyl acetate added to freshly reduced PtO_2 in ethyl acetate, stirred under O_2, at first slowly, after

5 min. more vigorously, and the product isolated after 80-100 min. → 3-methyl-2-(p-methoxyphenyl)-3-hydroperoxy-3H-pseudoindole. Y: 30 to 60%. B. Witkop, J. B. Patrick, and H. M. Kissman, B. *85*, 949 (1952).

Addition to Oxygen and Nitrogen OC ⇓ ON

Sodium hydroxide *NaOH*

Isoxazole ring opening ⊂

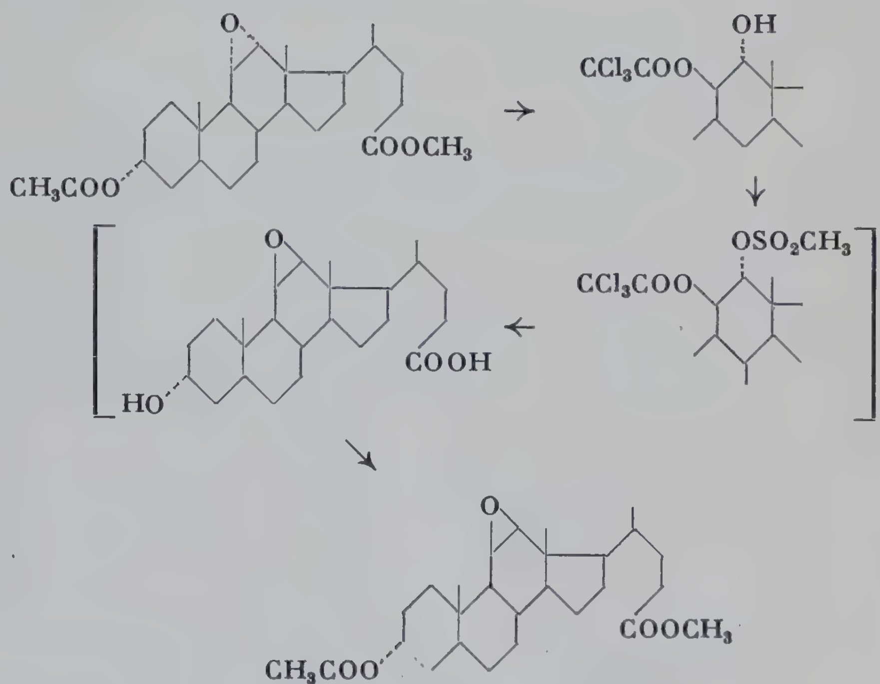
205. 

0.1 g. 6′-chloroquinolino(3′,4′:3,4)isoxazole (prepn. s. 375) and 2 *N* NaOH heated 2 hrs. at 95° → 0.1 g. 3-amino-6-chlorocinchoninic acid. F. e. s. D. W. Ockenden and K. Schofield, Soc. *1953*, 1915.

Addition to Oxygen and Carbon OC ⇓ OC

Without additional reagents *w.a.r.*

Epimerization of oxidosteroids ←
Double Walden inversion
Glycol monoesters from oxido compounds
Oxido compounds from glycol monoesters via glycol acetate methanesulfonates

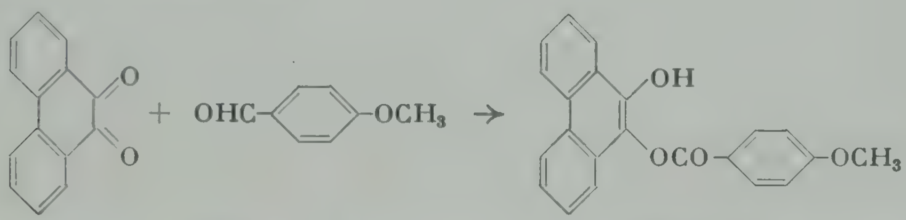
206. 

Methyl 3α-acetoxy-11,12α-oxidocholanate dissolved in a 0.56 *N* soln. of trichloroacetic acid in toluene, and allowed to stand 19 hrs. at room temp. → crude methyl 3α-acetoxy-11β-trichloroacetoxy-12α-hydroxycholanate (Y: 85-90%) allowed to stand with methanesulfonyl chloride in Pyridine at room temp. overnight, the crude product dissolved in ether, added dropwise to a boiling soln. of KOH in methanol, refluxed 1.5 hrs., the resulting crude 3α-hydroxy-11,12β-oxidocholanic acid allowed to react with diazomethane in ether, and the ester acetylated with acetic anhydride in pyridine → methyl 3α-acetoxy-11,12β-oxidocholanate (crude Y: 88%). Over-all Y: 45-55%. A. Fürst and R. Scotoni, Jr., Helv. *36*, 1410 (1953).

Irradiation ←

Quinol monoesters from quinones and aldehydes ←

07.



Phenanthrenequinone and anisaldehyde in benzene sealed under N_2 in a thin-walled bulb of soda-glass, shaken and irradiated with UV-light for 70 hrs. → 9-anisoyloxy-10-hydroxyphenanthrene. Y: ca. 100%. F. e. s. R. F. Moore and W. A. Waters, Soc. *1953*, 238.

Sodium hydroxide *NaOH*

Oxazolone ring opening

s. *5*, 117; also geometric isomers s. J. P. Lambooy, Am. Soc. *76*, 133 (1954)

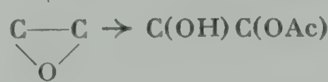
Sodium/alcohol *NaOR*

Dicarboxylic acid monoesters from dicarboxylic acid anhydrides

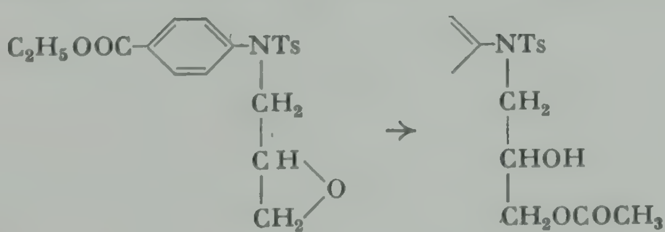
s. *9*, 368

Pyridine *C_5H_5N*

Glycol monoesters from oxido compounds



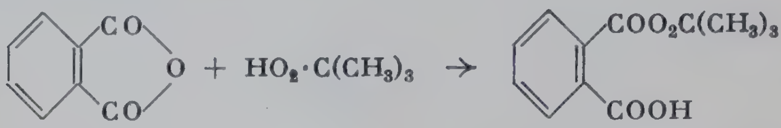
08.



A soln. of ethyl N-tosyl-N-(2,3-oxidopropyl)-p-aminobenzoate in glacial acetic acid containing 3 drops of pyridine heated 2 hrs. at 120° → crude ethyl N-tosyl-N-(3-acetoxy-2-hydroxypropyl)-p-aminobenzoate. Y: 88%. F. e. s. D. I. Weisblat et al., Am. Soc. 75, 3625 (1953).

Carboxyperoxycarboxylic acid esters from dicarboxylic acid anhydrides and hydroperoxides C

209.

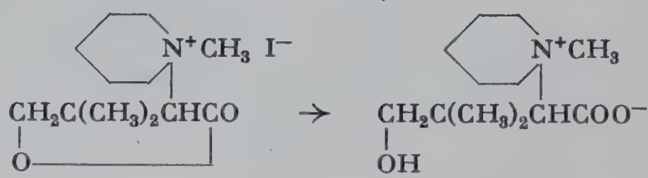


A mixture of 9 g. *tert*-butyl hydroperoxide, 14.8 g. phthalic anhydride, and pyridine allowed to stand 12 hrs. at room temp., finally warmed 10 min. at 65-68° → 20.2 g. 1-*tert*-butyl hydrogen 1-monoperphthalate. F. e. s. A. G. Davies, R. V. Foster, and A. M. White, Soc. *1953*, 1541.

Silver oxide *Ag_2O*

Hydroxybetaines from quaternary lactoneammonium salts

210.



An aq. soln. of α-(1-piperidyl)-β,β-dimethyl-γ-hydroxybutyrolactone methiodide shaken 17 hrs. with Ag_2O at room temp., filtered, and the filtrate shaken 6 hrs. with activated carbon to remove colloidal Ag_2O → α-(1-methyl-1-piperidyl)-β,β-dimethyl-γ-hydroxybutyric acid betaine. Y: 87%. H. Bretschneider and H. Haas, M. *82*, 427 (1951).

Aluminum alkoxide *$Al(OR)_3$*

Carboxylic acid esters from 2 aldehyde molecules Mixed Tishchenko reaction ←

211. The mixed ester from the acid of the aldehyde which undergoes the simple Tishchenko reaction most rapidly is formed in largest amounts. E. s. I. Lin and A. R. Day, Am. Soc. 74, 5133 (1952).

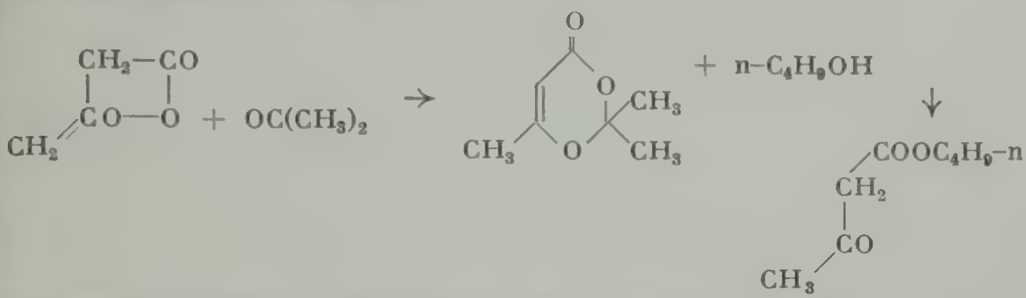
Phosphorus/hydriodic acid *P/HI*

s. Hydriodic acid/phosphorus

p-Toluenesulfonic acid *TsOH*

β-Ketocarboxylic acid esters from ketenedimers via 6-keto-1,3-diox-4-enes ←

2.

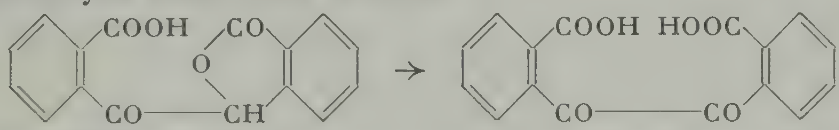


A mixture of 100 c.c. dry acetone, 100 c.c. diketene, and 0.5 g. p-toluenesulfonic acid refluxed 3 hrs. until the odor of diketene has disappeared → 2,2,4-trimethyl-6-keto-1,3-diox-4-ene (Y: 91% based on diketene; the yields are lower with larger amounts of catalyst) heated 3 hrs. at 100° with 1-butanol and a trace of p-toluenesulfonic acid → n-butyl acetoacetate (Y: 95%).—The diketene-ketone adducts may conveniently be used in place of diketene in many reactions. F. e. s. M. F. Carroll and A. R. Bader, Am. Soc. 75, 5400 (1953).

Potassium hypobromite *KOBr*

Ketocarboxylic acids from lactones C

3.



Aq. 33%-KOH added to a mixture of α-(o-carboxybenzoyl)phthalide and ethanol heated on a water bath, heating continued until a clear soln. results, more aq. KOH and, with agitation, Br added → benzil-2,2′-dicarboxylic acid (startg. m. f. 161). Y: 94%. F. e., with $KMnO_4$/Na_2CO_3, s. E. D. Bergmann and Z. Pelchowicz, Am. Soc. 75, 4281 (1953).

Hydrochloric acid *HCl*

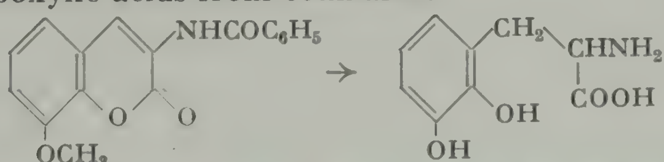
Pyran ring opening

s. *6*, 172; s. a. Org. Synth. *34*, 71 (1954)

Hydriodic acid/phosphorus *HI/P*

Reductive coumarin ring opening
α-Aminocarboxylic acids from coumarins

14.



A mixture of 3-benzamido-8-methoxycoumarin, glacial acetic acid, HI, and red P refluxed 2.5 hrs. in a stream of H_2 → 2,3-dihydroxyphenylalanine. Y: 66-90%. F. e. s. J. P. Lambooy, Am. Soc. 76, 133 (1954).

Potassium permanganate *$KMnO_4$*

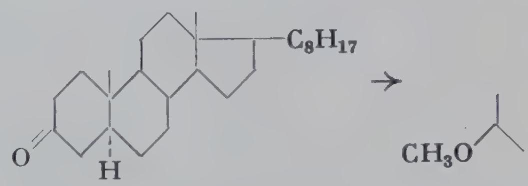
Ketocarboxylic acids from lactones

s. *9*, 213

Platinum oxide/hydrobromic acid *PtO_2/HBr*

Reductive methylation of steroid ketones CO → CH(OR)

215.



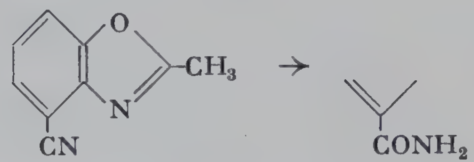
A suspension of 150 mg. cholestanone in methanol and a little 48%-HBr hydrogenated with PtO_2 until after 4 hrs. 1 mole H_2 has been absorbed → 110 mg. cholestanyl methyl ether. F. e. s. J. C. Babcock and L. F. Fieser, Am. Soc. *74*, 5472 (1952).

Addition to Nitrogen and Carbon OC ⇓ NC

Without additional reagents *w.a.r.*

Carboxylic acid amides from nitriles CN → $CONH_2$

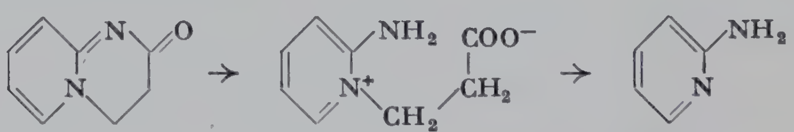
216.



2-Methyl-4-cyanobenzoxazole heated 3 hrs. in water at 180-190° in a sealed tube → 2-methylbenzoxazole-4-carboxylic acid amide. Y: 80%.— Lower yields are obtained by either a shorter or longer reaction time. C. Sannie and H. Lapin, Bl. *1952*, 369.

Pyrido[1,2-a]pyrimid-2-one ring opening C
Tert. amines from betaines

217.



A soln. of 0.30 g. 3,4-dihydro-2H-pyrido[1,2-a]pyrimidin-2-one in water refluxed 3 hrs. → 0.26 g. 2-imino-1(2H)-pyridinepropionic acid refluxed 2 hrs. in aq. 5%-NaOH → 2-aminopyridine (Y: 85%). R. Adams and I. J. Pachter, Am. Soc. *74*, 4906 (1952).

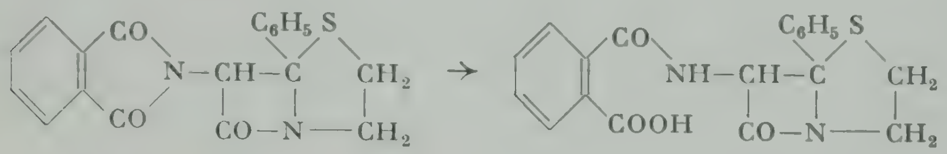
Sodium hydroxide *NaOH*

Dicarboxylic acid monoamides from dicarboxylic acid imides

s. 4, 157; s. a. A. Neuberger and J. J. Scott, Soc. *1954*, 1820

Selective hydrolysis with preservation of the penicillin ring system

218.



A soln. of 2-phenyl-α-phthalimido-2-thiazolidineacetic acid β-lactam in warm dioxane carefully cooled to room temp. to avoid crystallization, exactly the equivalent amount of 0.1 *N* NaOH soln. added, and the product isolated after 20 min. → α-(o-carboxybenzamido)-2-phenyl-2-thiazolidineacetic acid β-lactam. Y: 74%. J. C. Sheehan and J. J. Ryan, Am. Soc. *73*, 4367 (1951).

Nitric acid *HNO_3*

Acylguanylureas and acylbiurets from acyldicyanodiamides ←

219.

$$C_6H_5CONHC(NH_2){=}NC{\equiv}N$$

$$\swarrow \qquad\qquad \searrow$$

$$C_6H_5CONHC({=}NH)NHCONH_2 \dashrightarrow C_6H_5CONHCONHCONH_2$$

Benzoyldicyanodiamide (prepn. s. 511) and a slight excess of

4-10%-HCl refluxed until dissolved, and heating continued for several min. → benzoylguanylurea. Crude Y: 97.2%.

HNO_3 refluxed 1 hr. → benzoylbiuret (startg. m. f. 560). Crude Y: 77.4%.

F. e. s. P. Adams et al., J. Org. Chem. *17*, 1162 (1952).

Polyphosphoric acid *$H(PO_3H)_xOH$*

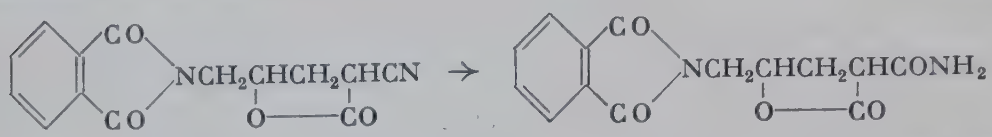
Carboxylic acid amides from nitriles $CN \rightarrow CONH_2$

220. Simple ar. and aliphatic nitriles are hydrolyzed to the corresponding amides in high yields by reaction with polyphosphoric acid for ca. 1 hr. at 110°.—E: Benzonitrile → benzamide. Y: 96%. F. e. s. H. R. Snyder and C. T. Elston, Am. Soc. *76*, 3039 (1954).

Sulfuric acid *H_2SO_4*

Carboxylic acid amides from nitriles CN → $CONH_2$

221.



2-Cyano-5-phthalimido-4-valerolactone dissolved in concd. H_2SO_4 cooled at 0°, and kept 24 hrs. at room temp.→2-carbamyl-5-phthalimido-4-valerolactone. Y: 93.6%. R. Gaudry and C. Godin, Am. Soc. *76*, 139 (1954); s. a. K. Scholz and L. Panizzon, Helv. *37*, 1605 (1954).

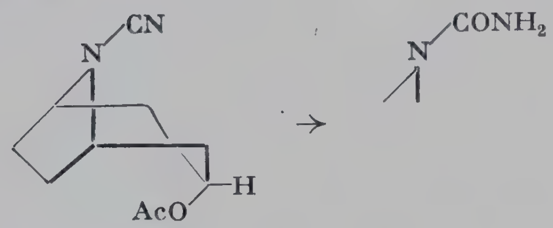
s. a. *9*, 583

Dicarboxylic acid amide esters from cyanocarboxylic acid esters

s. *9*, 559

Ureas from cyanamides >N·CN → >$NCONH_2$

222.



Concd. H_2SO_4 and a little water added to a soln. of crude N-cyanonortropine acetate in glacial acetic acid, allowed to stand overnight, the crude sulfuric acid salt dissolved in water, made alkaline with satd. K-carbonate soln., allowed to stand 15 min., and extracted with chloroform→N-carbamylnortropine acetate. Y: 75%. F. e. s. A. Nickon and L. F. Fieser, Am. Soc. *74*, 5566 (1952).

S-Thiocarbamic acid esters from thiocyanates SCN → $SCONH_2$

s. *7*, 196; s. a. R. Riemschneider and G. Orlick, M. *84*, 313 (1953)

Hydrochloric acid *HCl*

Acylguanylureas from acyldicyanodiamides CN → $CONH_2$

s. *9*, 219

Carbalkoxyguanylureas from carbalkoxydicyanodiamides

s. *9*, 562

Lactam ring opening C

s. *9*, 555

Aminodithiolcarbonic acid esters from thiazolines

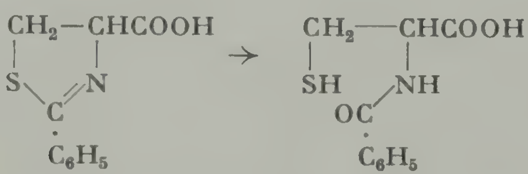
s. *9*, 705

Addition to Sulfur and Carbon OC $\Downarrow$ SC

Without additional reagents *w.a.r.*

Thiazoline ring opening C

223.



2-Phenylthiazoline-4-carboxylic acid added to boiling distilled water under N_2, and worked up after 15 min. $\rightarrow$ N-benzoylcysteine. Y: almost 100%. J. C. Crawhall and D. F. Elliott, Soc. *1952*, 3094.

Potassium hydroxide *KOH*

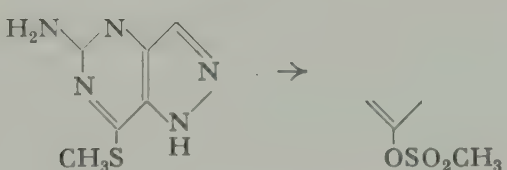
o-Mercaptophenylacetic acids from thianaphthenequinone 3-hydrazones

s. *9*, 121

Hydrogen peroxide/acetic acid *H_2O_2/CH_3COOH*

Sulfonic acid esters from thioethers SR $\rightarrow$ OSO_2R

224.



H_2O_2 added cautiously to a soln. of 4.5 g. 5-amino-7-methylthio-1,2,4,6-tetraazaindene in hot acetic acid, and heating continued at 90-95° for 1 hr. $\rightarrow$ 4 g. 5-amino-7-hydroxy-1,2,4,6-tetraazaindene methanesulfonate. F. L. Rose, Soc. *1952*, 3448.

Addition to Carbon OC⇓CC

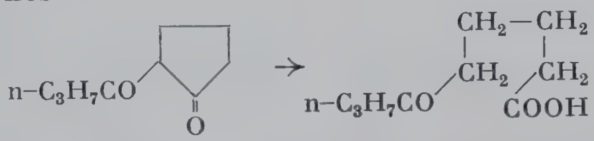
Sodium hydroxide *NaOH*

Alkoxyaldehydes from ethylenealdehydes C:C → CHC(OR)

225. 

Crotonaldehyde added slowly at -5^0 to stirred allyl alcohol containing aq. 40%-NaOH, acidified with acetic acid and phosphoric acid, then distilled → β-allyloxybutaldehyde. Y: 60%. F. e. s. R. H. Hall and E. S. Stern, Soc. *1952*, 4083.

Ketocarboxylic acids from cyclic acylketones

226. 

2-n-Butyrylcyclopentanone dissolved in 1.1 molar equivalents of 5%-NaOH soln. and refluxed 2 hrs. → δ-n-butyryl-n-valeric acid. Y: 78 to 90%. F. e. s. R. M. Manyik et al., Am. Soc. *75*, 5030 (1953).

Sodium hydroxide/hydrazine *$NaOH/H_2N{\cdot}NH_2$*
s. Hydrazine/sodium hydroxide

Potassium hydroxide *KOH*

Hydrolytic ring opening of isocyclics
s. *9*, 772

Sodium/alcohol *NaOR*

Ethers from ethylene derivatives C:C → CHC(OR)
s. *7*, 200; s. a. B. Englund, Org. Synth. *34*, 16 (1954)

Triethylamine *$(C_2H_5)_3N$*

O-Acetoacetylation $OH \rightarrow OCOCH_2COCH_3$
s. *9*, 954

Silver arylcarboxylate/iodine *ArCOOAg/I*

trans-Glycols from ethylene derivatives C:C → C(OH)C(OH)
s. *6*, 183; s. a. G. E. McCasland and E. C. Horswill, Am. Soc. *76*, 1654 (1954)

Barium hydroxide *$Ba(OH)_2$*

Ketocarboxylic acids from cyclic β-diketones
s. *7*, 202; s. a. B. *85*, 1061 (1952)

Mercuric oxide *HgO*

Ketones from acetylene derivatives C⋮C → $COCH_2$

s. *2*, 161; s. a. G. W. Stacy and R. A. Mikulec, Am. Soc. *76*, 524 (1954); W. J. Hickinbottom, A. A. Hyatt, and M. B. Sparke, Soc. *1954*, 2529; D. Papa, H. F. Ginsberg, and F. J. Villani, Am. Soc. *76*, 4441 (1954)

Mercuric oxide/boron fluoride *HgO/BF_3*

s. *9*, 933

Mercury-resin ←

α-Hydroxyketones from α,β-acetylenealcohols

s. *9*, 102

Amberlite ←

Cyanoethylation H → CH_2CH_2CN

s. *9*, 749

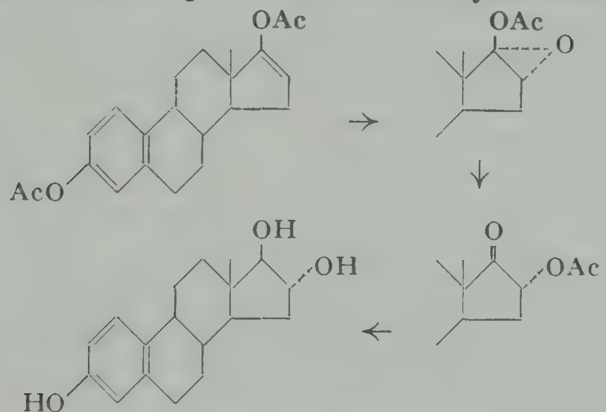
Peracetic acid *CH_3COO_2H*

Naphthalene ring opening

s. *4*, 168; s. a. G. A. Page and D. S. Tarbell, Org. Synth. *34*, 8 (1954)

Perbenzoic acid *$C_6H_5COO_2H$*

Stereoisomeric glycols from enolesters via 1-acoxy-1,2-oxido compounds and α-acoxyketones ←



A soln. of crude $\Delta^{1,3,5,16}$-estratetraene-3,17-diol diacetate in benzene allowed to react 15 hrs. with perbenzoic acid, the crude epoxide dissolved in cold acetic acid, a cold soln. of 70%-$HClO_4$ in acetic acid added, allowed to stand 0.5 hr. at room temp., the crude product dissolved in ether-benzene, a soln. of $LiAlH_4$ in dry ether added dropwise, and refluxed 1 hr. → estriol. Y: 66%.—By alkaline hydrolysis of the α-acoxyketone the procedure can be altered to afford an equally successful synthesis of 16β,17β-ring-D glycols. F. e., also isolation of the intermediates, direct reduction of the 1-acoxy-1,2-oxido compounds, and rearrangement by chromatography or heating above the melting point, s. N. S. Leeds, D. K. Fukushima, and T. F. Gallagher, Am. Soc. *76*, 2943 (1954).

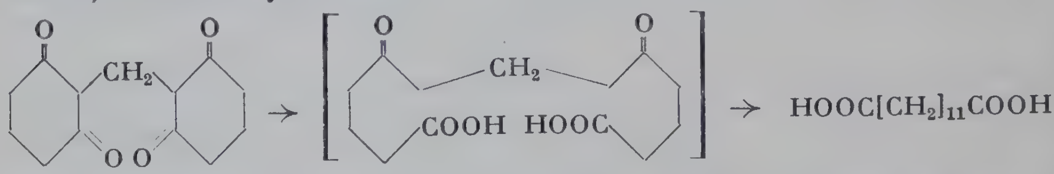
Perphthalic acid ←

α-Hydroxyketones from enolesters C:C(OAc) → C(OH)CO
s. *9*, 202

Hydrazine/sodium hydroxide *$H_2N \cdot NH_2/NaOH$*

Carboxylic acids from cyclic β-diketones
Acid cleavage
with subsequent Huang-Minlon reduction
Synthesis of long chain carboxylic
and α,ω-dicarboxylic acids

228.



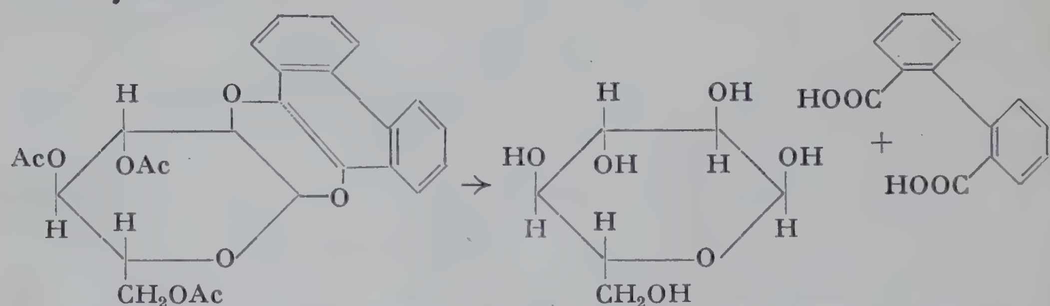
Methylenebisdihydroresorcinol (prepn. s. 806) and 85%-hydrazine hydrate added to a soln. of Na or NaOH in diethylene glycol, refluxed 30 hrs. after addition of abs. methanol to adjust the b. p. at 125°, methanol, water, and excess hydrazine hydrate distilled off until the temp. reaches 195°, and refluxing continued for 10-11 hrs. → brassylic acid. Y: 100%.—High yields are obtained because the hydrazine present reacts with the ketocarboxylic acid formed by acid cleavage, thus preventing side-reactions. Also monocarboxylic acids from 2-alkyl-1,3-cyclohexanediones s. H. Stetter et al., B. *85*, 290, 1061 (1952); *87*, 869 (1954); aminocarboxylic acids s. B. *87*, 1331; cf. H. Lettré and A. Jahn, B. *85*, 346 (1952).

Ozone O_3

Ozonides ←
s. *1*, 141/2; *2*, 167; s. a. J. E. Richmond and K. J. Altman, Am. Soc. *74*, 4368 (1952)

Removal of a protective group from the hydroxyl groups
at C-atoms 1 and 2 of aldopyranoses
Oxidative ring opening
Deacetylation

229.



An O_2-stream containing 2.3% O_3 passed into a mixture of phenanthrenehydroquinonetriacetyl-D-glucoside anhydride, ethyl acetate, acetic acid,

and a little water, at −15° for 30 min., finally at 0° for 10 min., and the crude product deacetylated by treating with Na-methoxide soln. in chloroform for 5 hrs. at 0° → glucose (Y: 78%) and diphenic acid (after hydrolyzing the resulting ester with KOH in methanol on a water bath) (Y: 75%). B. Helferich and E. v. Gross, B. 85, 531 (1952).

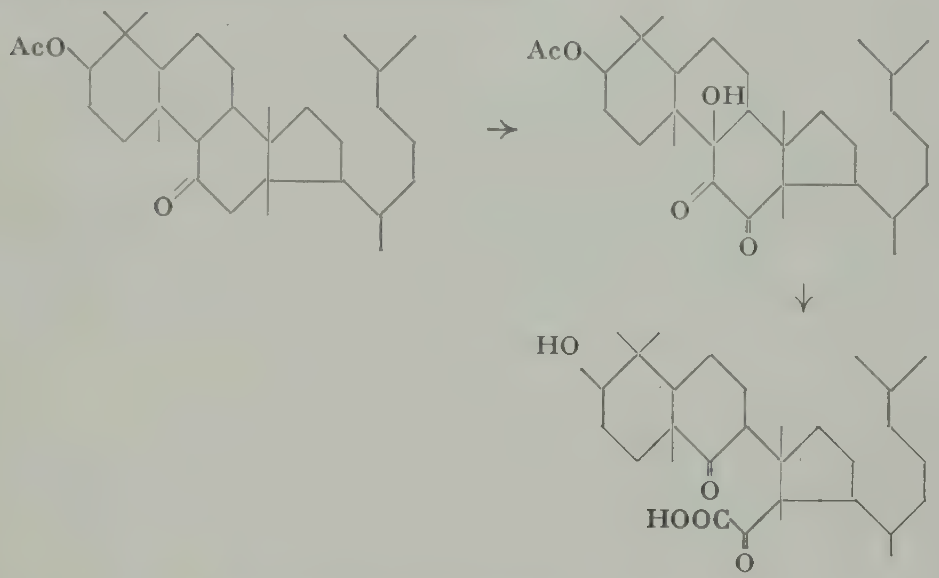
Oxidative indole ring opening

s. *2*, 168; s. a. D. W. Ockenden and K. Schofield, Soc. *1953*, 3440; J. L. Warnell and C. P. Berg, Am. Soc. *76*, 1708 (1954)

Hydrogen peroxide/potassium hydroxide *H_2O_2/KOH*

Oxidative ring opening
1,2,3-Hydroxydiketones from ketones

30.



A soln. of 500 mg. acetoxylanostanone in dioxane heated with SeO_2 at 180° in a sealed tube for 4 hrs. → 310 mg. dihydroxydiketone monoacetate, 970 mg. dissolved in methanol, KOH in methanol-water then 30%-H_2O_2 added, and the product isolated after 20 hrs. → 800 mg. hydroxydiketocarboxylic acid. W. Voser et al., Helv. *35*, 2065 (1952).

Sulfuric acid *H_2SO_4*

Ethers from ethylene derivatives C:C → CHC(OR)

31. $CH_3COCH{=}CH_2 + CH_3OH \rightarrow CH_3COCH_2CH_2OCH_3$

Methyl vinyl ketone in dry methanol added below 30° to a stirred soln. of a small amount of concd. H_2SO_4 in methanol, and the product isolated after 2 hrs. at room temp. → 1-methoxy-3-butanone. Y: 83-90%. —Use of BF_3-HgO catalyst gave erratic yields. M. S. Newman, J. Waltcher, and H. F. Ginsberg, J. Org. Chem. *17*, 962 (1952).

Acoxy compounds from ethylene derivatives C:C → CHC(OCOR)
s. *9*, 232

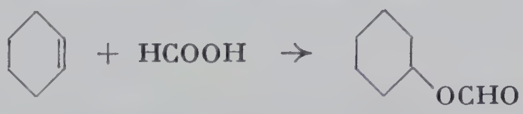
Carboxylic acid esters from ethylene derivatives
s. *7*, 212; s. a. Org. Synth. *34*, 26 (1954)

Sulfuric acid/formic acid *H_2SO_4/HCOOH*

Hydration of ethylene derivatives C:C → CHC(OH)
s. *9*, 790

Perchloric acid *$HClO_4$*

Acoxy compounds from ethylene derivatives C:C → CHC(OCOR)

232. 

Cyclohexene added to 90%-formic acid containing a little $HClO_4$, and kept 20 min. at 100° → cyclohexyl formate. Y: 90%. F. e. s. G. F. Bloomfield, Soc. *1953*, 3329.
H_2SO_4 is a slightly less efficient catalyst when anhydrous formic acid is used but the efficiency of these catalysts is reversed with 90%-formic acid. Acetic acid, catalyzed by $HClO_4$, also adds to the double bond but at a lower rate and less completely than formic acid. E. s. H. B. Knight, R. E. Koos, and D. Swern, Am. Soc. *75*, 6212 (1953).

Periodate *IO_4^-*

Oxidative ring opening

233. Resistance of a compound to periodate oxidation is not in itself proof of the absence of vicinal hydroxyl groups. E. s. B. H. Alexander, R. J. Dimler, and C. L. Mehltretter, Am. Soc. *73*, 4658 (1951).

Hydrochloric acid *HCl*

Protection of hydroxyl groups by formation of tetrahydro-2-pyranyl ethers C:C → CHC(OR)
s. *5*, 144; steroids s. A. C. Ott, M. F. Murray, and R. L. Pederson, Am. Soc. *74*, 1239 (1952); E. Elisberg, H. Vanderhaeghe, and T. F. Gallagher, Am. Soc. *74*, 2814 (1952)

Hydrobromic acid *HBr*

2,3,5-Trialkoxytetrahydrofurans C:C → CHC(OR)

234. 

1 mole HBr introduced by a stream of N_2 during 3 hrs. into a cooled soln. of 2,5-diethoxy-2,5-dihydrofuran in abs. ethanol → 2,3,5-triethoxytetrahydrofuran (startg. m. f. 381). Y: 68%. F. e. and methods, also with exchange of alkoxy groups, s. A. Stoll, A. Lindenmann, and E. Jucker, Helv. *36*, 1500 (1953).

Osmium tetroxide *OsO_4*

Glycols from ethylene derivatives C:C → C(OH)C(OH)

s. *1*, 147-9; *2*, 177/8; s. a. R. Hirschmann et al., Am. Soc. *76*, 4013 (1954)

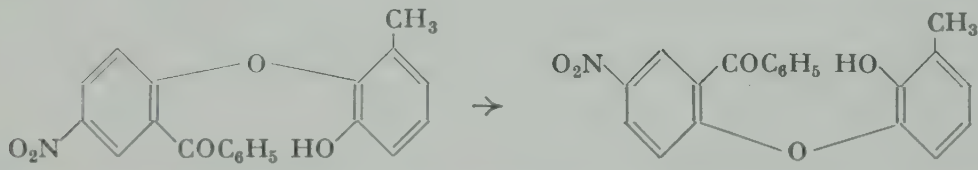
Rearrangement

Hydrogen/Oxygen Type OC⤶∩HO

Alkali hydroxide ←

Smiles rearrangement ←

5.



A trace of *N* NaOH added at room temp. to an almost satd. soln. of 2-(2″-hydroxy-6″-methylphenoxy)-5-nitrobenzophenone in methanol, and the product allowed to crystallize → 2-(2″-hydroxy-3″-methylphenoxy)-5-nitrobenzophenone. Y: 90%. F. e. s. J. D. Loudon and J. A. Scott, Soc. *1953*, 265; with aq. 5%-KOH s. Soc. *1950*, 55.

Hydrogen/Carbon Type OC⤶∩HC

Boron fluoride *BF_3*

Ketones from oxido compounds CH—CH (—O—) → CH_2CO

cf. Synth. Meth. *8*, 192

36. Epimerization and isomerization can be avoided by stopping the reaction at the optimum time by addition of pyridine, e. g. an 80% Y of 3β-acetoxy-22.23-dibromo-9β-ergost-7-en-11-one is obtained after 15 min. in toluene at -35^0. F. e. s. J. Elks et al., Soc. *1953*, 2933.

Formic acid *HCOOH*

Oxo compounds from glycol monoethers ←

s. *7*, 750; s. a. S. Winstein, C. R. Lindegren, and L. L. Ingraham, Am. Soc. *75*, 155 (1953)

Titanium tetrachloride *$TiCl_4$*

α- from β-Glycosides

s. *6*, 193; s. a. R. E. Reeves and L. W. Mazzeno, Jr., Am. Soc. *76*, 2219 (1954)

Sulfur *S*

Willgerodt reaction

Carboxylic acid amides from ketones $CONH_2$

s. *3*, 139; with heterocyclics, influence of temp. s. J. A. Blanchette and E. V. Brown, Am. Soc. *74*, 1066 (1952)

Carboxylic acid amides from oxido compounds

237.

Styrene oxide, sulfur, yellow NH_4-polysulfide, and dioxane heated 7 hrs. at ca. 170° in a sealed tube → phenylacetamide. Y: 87%. Also from other compound classes s. R. T. Gerry and E. V. Brown, Am. Soc. *75*, 740 (1953).

Ammonium polysulfide *$(NH_4)_2S_x$*

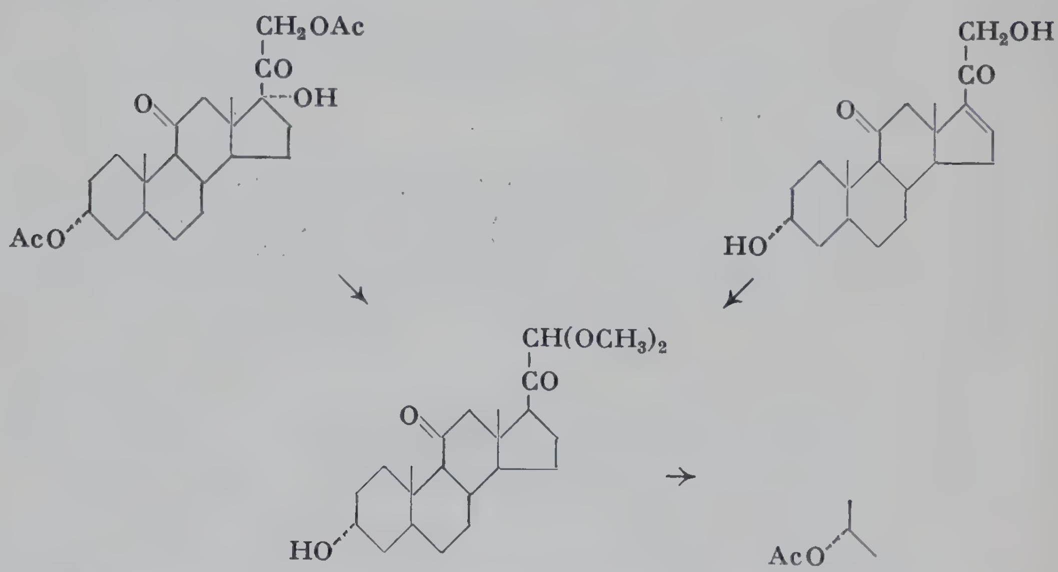
Carboxylic acid amides from methyl ketones

s. *1*, 151/2; *2*, 180/a; s. a. Yu. A. Baskakov and N. N. Mel'nikov, Ж. *23*, 865 (1953); C. A. *48*, 4477 a

Hydrochloric acid *HCl*

Formation of α-ketoacetals with rearrangement ←

238.



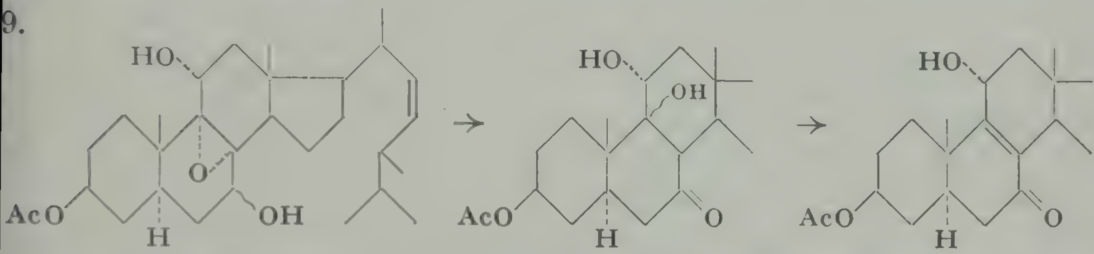
3α,21-Diacetoxy-17α-hydroxypregnane-11,20-dione in HCl-methanol-chloroform allowed to stand 48 hrs. at room temp., and the crude product reacetylated by keeping 5 hrs. at room temp. with acetic anhydride-pyridine → 3α-acetoxy-21,21-dimethoxypregnane-11,20-dione

(Y: 87%: from 3α,21-dihydroxy-Δ^{16}-pregnene-11,20-dione by similar treatment, Y: 71%) and unconverted startg. m. (Y: 5%). F. e. s. V. R. Mattox, Am. Soc. *74*, 4340 (1952); from α-acoxy-α'-hydroxyketones s. a. D. Taub et al., Am. Soc. *76*, 4094 (1954).

Hydrobromic acid *HBr*

α,β-Ethyleneketones from oxidoalcohols via β-hydroxyketones ←
Partial dehydration

9.



Aq. 48%-HBr added to a soln. of 3β-acetoxy-7ξ,11α-dihydroxy-8α,9α-oxido-Δ^{22}-ergostene, and the product isolated after ca. 45 min. → 3β-acetoxy-9ξ,11α-dihydroxy-7-oxo-Δ^{22}-ergostene (Y: almost 100%) dissolved in dioxane, treated with aq. 10%-KOH whereby two phases are formed, and refluxed 2.5 days → 3β,11α-dihydroxy-7-oxo-$\Delta^{8,22}$-ergostadiene (Y: almost 100%). H. Heusser et al., Helv. *35*, 936 (1952).

Via intermediates *v.i.*

Willgerodt-Kindler reaction $COCH_3 \rightarrow CH_2COOH$
cf. Synth. Meth. *3*, 141

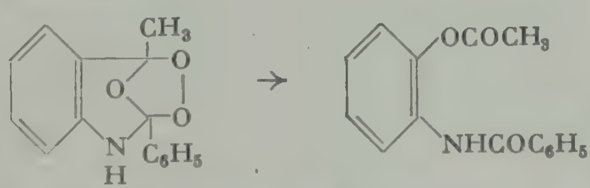
0. **Removal of sulfur.** Traces of sulfur may be detrimental in subsequent reactions. However, the acids can be made sulfur-free by heating an alkaline soln. of the acid with Raney-Ni catalyst. E. s. E. R. Shepard et al., J. Org. Chem. *17*, 568 (1952).
One-step procedure s. J. S. Stinson and R. V. Lawrence, J. Org. Chem. *19*, 1047 (1954).

Oxygen/Oxygen Type OC⌒OO

Acetic anhydride *$(CH_3CO)_2O$*

Rearrangement of N-heterocyclic ozonides ←

1.



Concd. H_2SO_4 added dropwise to 2-phenylskatole ozonide until no further precipitation is observed, the ozonide sulfate centrifuged, the

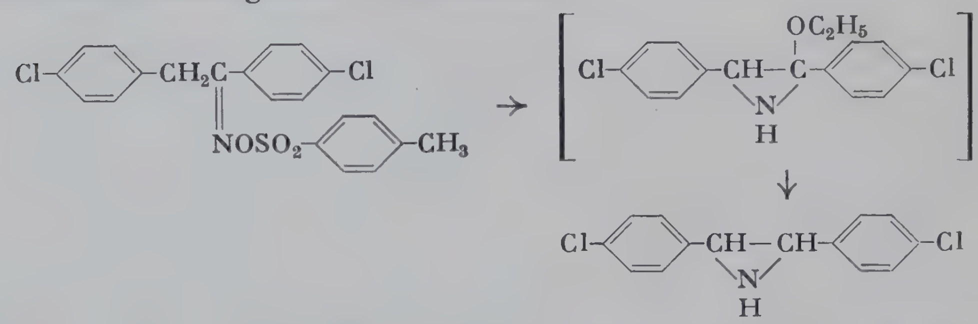
ether decanted, then acetic anhydride added dropwise with cooling and stirring → N-benzoyl-O-acetyl-o-aminophenol. Y: 93%.—Use of propionic anhydride gives the same product. B. Witkop and J. B. Patrick, Am. Soc. *74*, 3861 (1952).

Oxygen/Nitrogen Type — OC ⌒ ON

Potassium/alcohol — *KOR*

Ethylenimines from oxime sulfonates via Neber rearrangement intermediate ←

242.

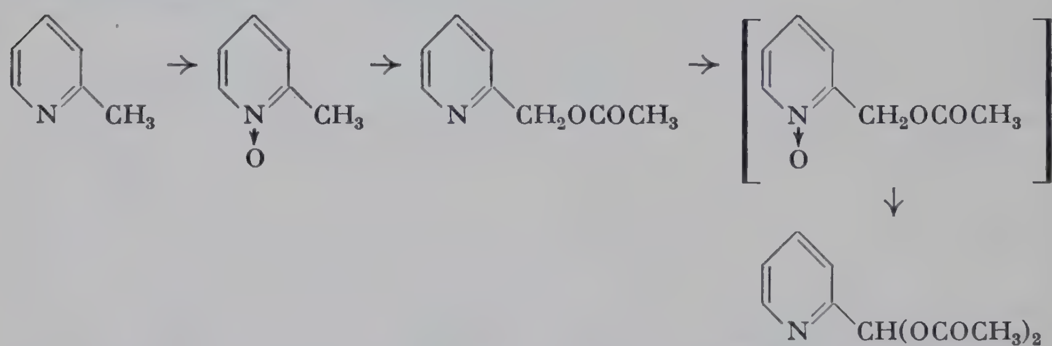


A soln. of K in abs. ethanol added at 0° during 2 min. to a suspension of p,p′-dichlorodesoxybenzoinoxime tosylate (prepn. s. 179) in abs. ethanol, ice-cooled and vigorously beaten for 5 hrs., filtered, the filtrate extracted with ether, and the dry ether soln. reduced with $LiAlH_4$ → p,p′-dichlorodiphenylethylenimine. Y: 60%. F. e. s. M. J. Hatch and D. J. Cram, Am. Soc. *75*, 38 (1953).

Acetic anhydride — *$(CH_3CO)_2O$*

N-Heterocyclic carbinols and aldehydes via N-oxides ←

243.



A mixture of 2-picoline, acetic acid, and aq. 30%-H_2O_2 heated 3 hrs. at 70-80°, more H_2O_2 added, and heated another 9 hrs. → 2-picoline N-oxide (Y: 83%) added dropwise to gently boiling acetic anhydride, and refluxing continued for 15 min. → 2-pyridinemethanol acetate (Y: 78%) similarly via the N-oxide in one step → 2-pyridinealdehyde diacetate (Y: 46%). F. e., with and without isolation of the intermediate N-oxide, s. V. Boekelheide and W. J. Linn, Am. Soc. *76*, 1286 (1954), s. a. O. H. Bullitt, Jr., and J. T. Maynard, Am. Soc. *76*, 1370 (1954).

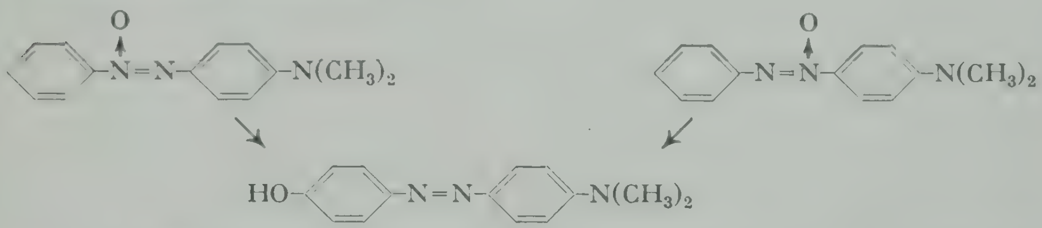
Polyphosphoric acid *P(PO$_3$H)$_x$OH*

Lactams from oximes ←
Ring expansion

s. *7*, 224; s. a. Am. Soc. *76*, 3651 (1954)

Sulfuric acid *H$_2$SO$_4$*

Hydroxyazo from azoxy compounds ←
Wallach transformation

244. 

α- or β-p-Dimethylaminoazoxybenzene heated 10 min. in concd. H_2SO_4 in a water bath → p′-dimethylamino-p-hydroxyazobenzene. Y: almost 100%. W. Anderson, Soc. *1952*, 1722.

Hydrochloric acid *HCl*

Beckmann rearrangement ←
Carboxylic acid amides from oximes

s. *4*, 184; s. a. R. E. and G. G. Lyle, J. Org. Chem. *18*, 1058 (1953)

Oxygen/Carbon Type **OC↶OC**

Perchloric acid *HClO$_4$*

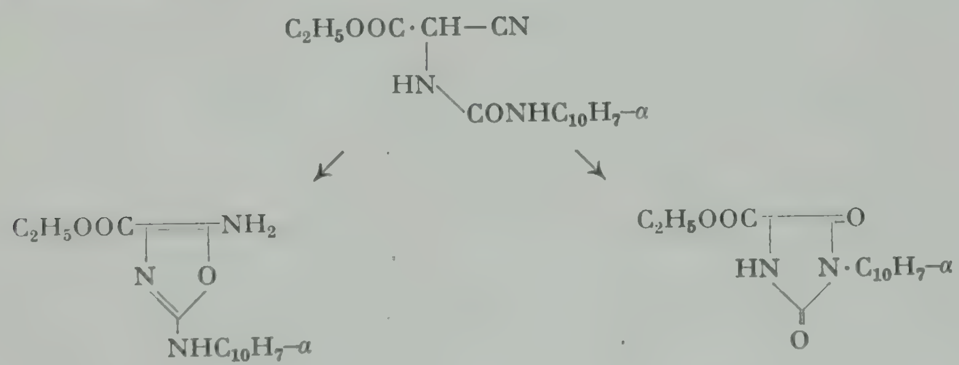
Ketones from oxido compounds ←
with rearrangement

s. *9*, 227

Nitrogen/Carbon Type **OC↶NC**

Sodium/alhohol *NaOR*

Oxazoles and hydantoins ○
from α-ureidonitriles

245. 

N-Carbethoxycyanomethyl-N′-α-naphthylurea

refluxed 2 hrs. with a soln. of Na in dry ethanol → ethyl 5-amino-2-α-naphthylaminoxazole-4-carboxylate. Y: 94%.

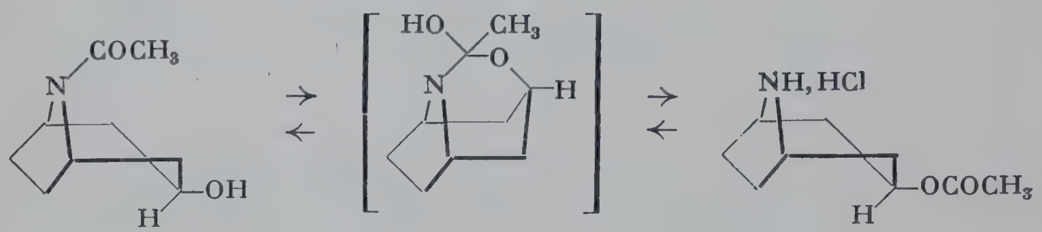
refluxed 1 hr. with ethanolic 10%-HCl → 5-carbethoxy-3-α-naphthylhydantoin. Y: 90%.

F. e. also tautomeric oxazolines, s. A. H. Cook and G. D. Hunter, Soc. *1952*, 3789.

Hydrochloric acid *HCl*

Acyl group migration as used for determination of configuration NAc → OAc

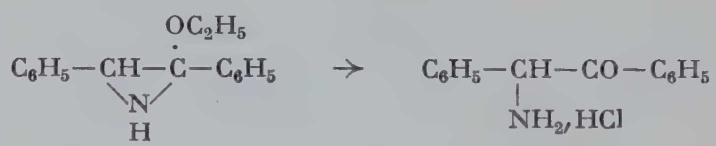
246.



A soln. of N-acetylnorpseudotropine in anhydrous dioxane rapidly satd. with dry HCl, refluxed 8 hrs., and evaporated to dryness with the help of a jet of air → O-acetylnorpseudotropine hydrochloride (Y: 87%) dissolved in water, treated with K-carbonate, after 10 min. heated on a steam bath for 15 min. → N-acetylnorpseudotropine (Y: 76%).— The migration occurs with retention of configuration. No migration takes place in the transoid tropine analogs. F. e. s. A. Nickon and L. F. Fieser, Am. Soc. *74*, 5566 (1952); s. a. G. Fodor et al., Soc. *1953*, 721, 724.

α-Aminoketones from 2-alkoxyethylenimines

247.



An ethereal soln. of 2,3-diphenyl-2-ethoxyethylenimine shaken with 2 *N* HCl, and the product isolated from the aq. layer → desylamine hydrochloride. Y: 90%. M. J. Hatch and D. J. Cram, Am. Soc. *75*, 38 (1953).

Sulfur/Carbon Type
OC↶SC

Acetic acid *CH_3COOH*

O-S Acyl migration OAc → SAc

12 g. *trans*-2-acetylthiocyclohexanol heated 13 hrs. at 100° in the presence of a little acetic acid → 11 g. *trans*-2-mercaptocyclohexyl acetate. L. W. C. Miles and L. N. Owen, Soc. *1952*, 817.

Carbon/Carbon Type
OC↶CC

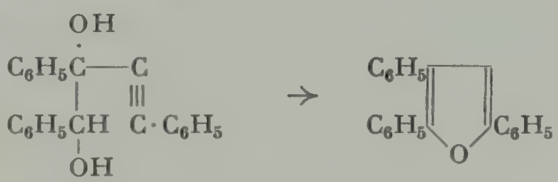
Sodium hydroxide *NaOH*

Ketones from 2-ethylenealcohols ←
Steroids

s. *8*, 202; s. a. J. Romo et al., J. Org. Chem. *19*, 1509 (1954)

Mercuric chloride *$HgCl_2$*

Furans from acetyleneglycols ○



A satd. soln. of 1,2,4-triphenyl-3-butyne-1,2-diol in 96%-alcohol containing $HgCl_2$ heated 8 hrs. at 100° in a sealed tube → 2,3,5-triphenylfuran. Y: 85-90%. E. D. Venus-Danilova and V. M. Al'bitskaya, Ж. *22*, 816 (1952); C. A. *47*, 3266 c.

Sulfuric acid *H_2SO_4*

α,β-Ethylenecarboxylic acid esters ←
from alkoxyacetylenealcohols

s. *6*, 200; s. a. H. Kappeler, Helv. *37*, 957 (1954); also α,β-hydroxycarboxylic acid esters s. G. E. Arth et al., Am. Soc. *76*, 1715 (1954)

Exchange

Hydrogen ↑
OC⇅H

Electrolysis ↯

Carboxylic acids from alcohols CH_2OH → COOH

s. *4*, 187; acetylenecarboxylic acids s. V. Wolf, B. *87*, 668 (1954)

Mercuric acetate $(CH_3COO)_2Hg$

Acylating oxidation H → OAc

s. *5*, 162; corrections regarding allyl rearrangement and mechanism s. A. *581*, 59 (1953)

Nitrobenzene/chromic acid $C_6H_5NO_2/CrO_3$

s. Chromic acid/nitrobenzene

Lead tetraacetate $(CH_3COO)_4Pb$

Furanones from furans ←

250.

2-Acetoxyfuran added at once with stirring to a suspension prepared from red lead oxide, glacial acetic acid, and acetic anhydride, the temp. kept 30 min. at 20-25°, then raised to 40°, and kept 30 min. at 40-45° → 5-acetoxy-2(5H)-furanone. Y: 88%. N. Elming and N. Clauson-Kaas, Acta Chem. Scand. *6*, 565 (1952).

Oxidations with

Potassium nitrosodisulfonate $ON(SO_3K)_2$

Quinones from phenols ←

s. *8*, 206; s. a. B. *87*, 1236 (1954); cf. B. *87*, 1251 (1954)

Potassium persulfate $K_2S_2O_8$

o-Aminosulfuric acid esters from ar. amines H → OSO_3K

s. *9*, 203

Selenium dioxide SeO_2

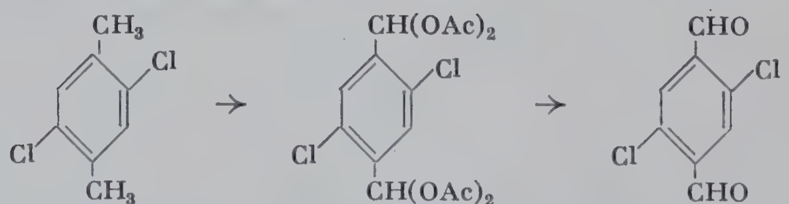
1,2,3-Hydroxydiketones from ketones ←

s. *9*, 230

Chromic acid CrO_3

Aldehydes from hydrocarbons (methyl groups) via 1,1-diacoxy compounds CH_3 → CHO

251.

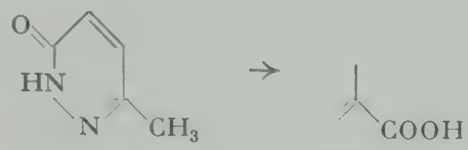


2,5-Dichloro-p-xylene dissolved in a stirred mixture of acetic acid, acetic anhydride, and H_2SO_4, cooled to 5°, CrO_3 added during 2.5 hrs.

at such a rate as to keep the temp. at 5-12°, and stirring continued at 10-15° for 4 hrs. → 2.5-dichloroterephthaldehyde tetraacetate (Y: 37%) added to a mixture of ethanol, water, and H_2SO_4, and refluxed 1.5 hrs. → 2.5-dichloroterephthaldehyde (Y: 86%). F. e. s. J. R. Naylor, Soc. *1952*, 4085.

Carboxylic acids from hydrocarbons (methyl groups) $CH_3 \rightarrow COOH$

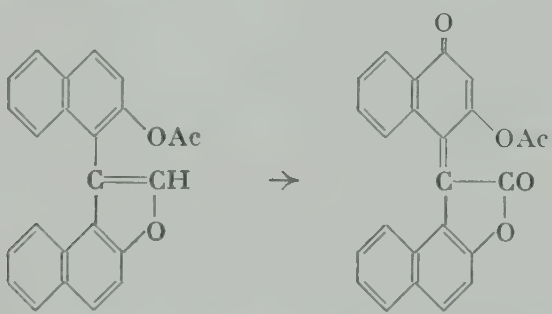
2.



Finely powdered $K_2Cr_2O_7$ added at 30-50° to a stirred soln. of 6-methyl-3-pyridazone in concd. H_2SO_4, and stirring continued for 2 hrs. → 3-pyridazone-6-carboxylic acid monohydrate. Y: 68-72%. R. F. Homer et al., Soc. *1948*, 2195; s. a. J. A. King and F. H. McMillan, Am. Soc. *74*, 3222 (1952).

Oxidation of 3-arylfurans ←

3.

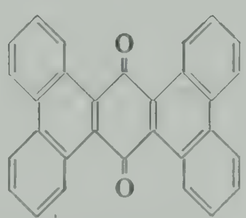


A soln. of CrO_3 in glacial acetic acid added dropwise with shaking at room temp. during 15 min. to a soln. of 1-(2-acetoxy-1-naphthyl)-naphtho[2.1-b]furan in glacial acetic acid, and allowed to stand overnight → 1-(2-acetoxy-4-oxo-1(4H)-naphthalidene)naphtho[2.1-b]furan-2(1H)-one. Y: 68%. F. e. s. O. Dischendorfer and H. Lapaine, M. *82*, 397 (1951).

Chromic acid/nitrobenzene *$CrO_3/C_6H_5NO_2$*

Quinones from hydrocarbons ←

54.



$Na_2Cr_2O_7$ in acetic acid added slowly to a warm soln. of tetrabenz[a,c,h,j]anthracene (prepn. s. 937) in nitrobenzene, and refluxed 18 hrs. →

tetrabenz[a,c,h,j]anthracene-9,18-dione. Y: 52%. P. Lambert and R. H. Martin, Bl. Soc. chim. Belg. *61,* 124 (1952).

tert-Butyl chromate ←

α,β-Ethyleneketones $CH_2 \rightarrow CO$
from ethylene derivatives

s. *8,* 208; terpene derivatives s. G. Dupont, R. Dulou, and O. Mondou, Bl. *1953,* 60

tert-Butyl hypochlorite $(CH_3)_3C{\cdot}OCl$

Carboxylic acid esters $2\,RCH_2OH \rightarrow RCOOCH_2R$
from 2 alcohol molecules

s. *9,* 363

Potassium permanganate $KMnO_4$

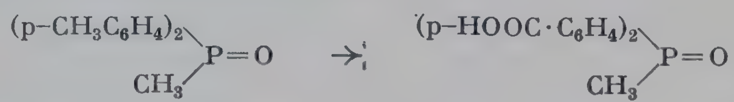
Carboxylic acids from alcohols $CH_2OH \rightarrow COOH$

in aq. NaOH s. *3,* 153; in acetone-water s. W. R. Brasen and C. R. Hauser, J. Org. Chem. *18,* 806 (1953)

Potassium permanganate/pyridine $KMnO_4/C_5H_5N$

Carboxylic acids $CH_3 \rightarrow COOH$
from hydrocarbons (methyl groups)

255.



Water added to a soln. of methyldi-p-tolylphosphine oxide (prepn. s. 196) in pyridine, heated on a steam bath, $KMnO_4$ added portionwise during 5 hrs. at a rate to maintain refluxing, more water added to keep the mixture from becoming pasty, and heating continued for 2 hrs. → bis-(p-carboxyphenyl)methylphosphine oxide. Y: 88%. F. e. s. P. W. Morgan and B. C. Herr, Am. Soc. *74,* 4526 (1952).

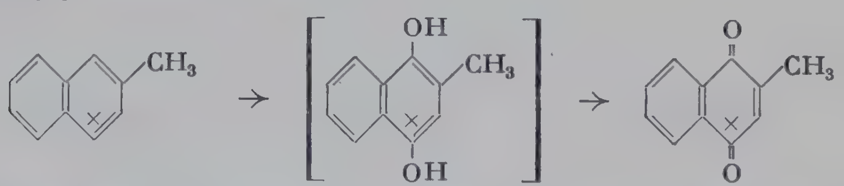
Via intermediates *v.i.*

α-Acoxyethylenes from ethylene derivatives ←
via glycol monoesters

s. *7,* 239; s. a. J. Org. Chem. *19,* 1509 (1954)

Quinones from hydrocarbons ←
via quinols

256.



A soln. of 2-methylnaphthalene-4-C^{14} in CCl_4 oxidized with $Na_2Cr_2O_7$ in H_2SO_4-water, the CCl_4-layer removed, the aq. layer extracted with

CCl_4 and ether, this CCl_4-ether layer extracted with aq. $NaOH$-$Na_2S_2O_4$, the unoxygenated fraction remaining in the CCl_4 reoxidized in the same way, and the hydroquinone from both oxidations oxidized with Ag_2O in the presence of a small amount of anhydrous $MgSO_4$ → 2-methyl-1,4-naphthoquinone-4-C^{14}. Y: 48-52%. L. Li and W. H. Elliott, Am. Soc. 74, 4089 (1952); method s. J. Hyman and C. F. Peter, U. S. P. 2,402,226.

Carboxylic acids from methyl groups via styryl derivatives $CH_3 \rightarrow COOH$

s. *3*, 156; s. a. M. Häring, B. Prijs, and H. Erlenmeyer, Helv. *37*, 1339 (1954)

Oxygen ↿ OC⇅O

Without additional reagents *w.a.r.*

Carboxylic acid esters from carboxylic acid anhydrides $(RCO)_2O \rightarrow RCOOR$

7. $$(CF_3CO)_2O + HOC_6H_5 \rightarrow CF_3COOC_6H_5 + CF_3COOH$$

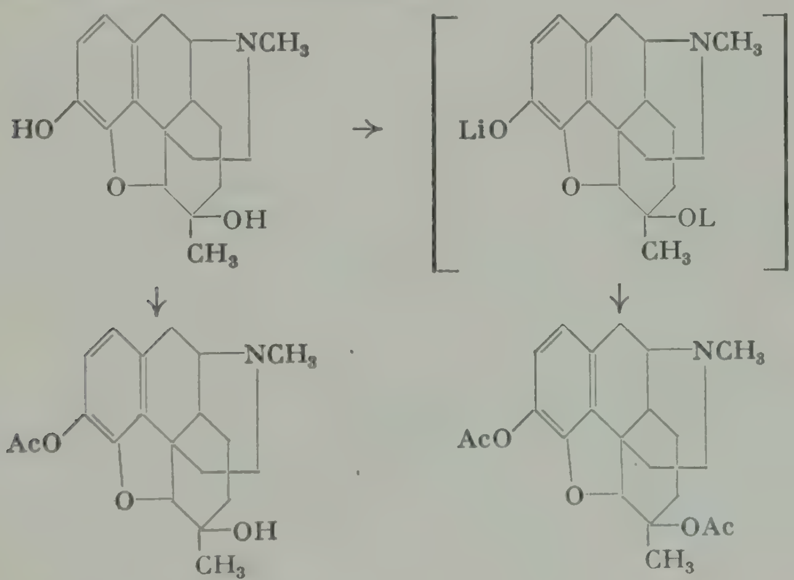
Trifluoroacetic anhydride added dropwise with stirring at 120° to a slight excess of phenol → phenyl trifluoroacetate. Y: 95%.—Other methods to prepare ar. esters of fluorocarbon acids were not successful. F. e. s. R. F. Clark and J. H. Simons, Am. Soc. *75*, 6305 (1953).

Potassium/nickel-silica *K/Ni-SiO₂*
s. Nickel-silica/potassium

Methyllithium *CH_3Li*

Acylation of slow reacting hydroxyl groups
Selective acylation of phenol groups $OH \rightarrow OAc$

8.



6-Methyldihydromorphine

allowed to react with acetic anhydride in dry pyridine → 3-acetyl-6-methyldihydromorphine. Y: high.

treated dropwise at 0-5° with excess methyl-Li, then excess acetic anhydride added, refluxed 30 min., and allowed to stand overnight → 3,6-diacetyl-6-methyldihydromorphine. 0.54 g. from 1 g.

H. D. Brown et al., Am. Soc. *75*, 6238 (1953); with methyl-Li s. a. T. D. Perrine, J. Org. Chem. *18*, 898 (1953).

Potassium acetate *CH_3COOK*

Enolesters from aldehydes CHCHO → C:CH(OAc)

s. *6*, 575; s. a. P. Bladon et al., Soc. *1952*, 4890

Ammonium and amine salts ←

Esterification of acid sensitive compounds RCOOR′

259. A mixture of NH_4-acetate, either solid or in a concd. aq. soln., and 2.5 moles n-butanol refluxed 7.5 hrs. at 118-122° with a water-separating trap → n-butyl acetate. Conversion: 64%.—This method may be useful for preparing esters from acid-sensitive alcohols and organic acids as well as for preparing esters of certain fermentation acids. F. e., also with amine salts, s. E. M. Filachione, E. J. Costello, and C. H. Fisher, Am. Soc. *73*, 5265 (1951); Ind. Eng. Chem. *44*, 2189 (1952).

Triethylamine *$(C_2H_5)_3N$*

Carboxylic acid esters from carboxylic acids via mixed carboxylic acid anhydrides COOH → COOR

s. *9*, 453

Pyridine *C_5H_5N*

Formoxy compounds OCHO

s. *9*, 17

Acetylation of alcohols OH → OAc

s. *2*, 194/5; large batches of steroids s. H. H. Inhoffen, H. Jahnke, and P. Nehring, B. *87*, 1154 (1954)

Selective acetylation

of sec. **hydroxyl groups** s. *6*, 206; of prim. hydroxyl groups s. Huang-Minlon, R. Tull, and J. Babcock, Am. Soc. *76*, 2396 (1954)

of phenol groups

s. *9*, 258

Cadmium ion/hydrochloric acid *Cd^{++}/HCl*

Acetylation of sugar acids

s. 5, 169; s. a. D. G. Doherty, J. Biol. Chem. *201*, 857 (1953)

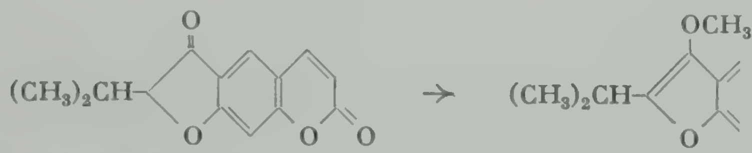
Boron fluoride *BF_3*

Lactolesters from lactols ←

s. *9*, 272

Aluminum chloride *$AlCl_3$*

Enolethers CHCO → C:C(OR)

0. 

$AlCl_3$ added portionwise to a gently refluxing soln. of oreoselone in anhydrous methanol, then heated 3 hrs. at a bath temp. of 100° → peucedanin. Y: high. H. Schmid and A. Ebnöther, Helv. *34*, 1982 (1951).

Methoxyacetylene *$HC{\vdots}C{\cdot}OCH_3$*

Acid anhydrides ←

1. $$2\ C_6H_5CH_2COOH \rightarrow (C_6H_5CH_2CO)_2O$$

$$2\ p\text{-}CH_3C_6H_4SO_3H \rightarrow (p\text{-}CH_3C_6H_5SO_2)_2O$$

Methoxyacetylene added to phenylacetic acid in methylene dichloride, and allowed to stand 18 hrs. at 20° → phenylacetic anhydride. Y: 96%. —Similarly with efficient cooling: p-Toluenesulfonic anhydride. Y: 52%.—This method seems to be the mildest yet devised for converting an acid into its anhydride. F. e. s. G. Eglinton et al., Soc. *1954*, 1860.

Phosphorus oxychloride *$POCl_3$*

Carboxylic acid phenolesters COOH → COOR

s. *8*, 223; s. a. G. H. Daub and W. S. Johnson, Org. Synth. *34*, 44 (1954).

Thionyl chloride or phosphorus trichloride *$SOCl_2$ or PCl_3*

Acylation of alcohols OH → OAc

α-Formoxyketones from α-hydroxyketones

2. $$\begin{array}{l} C_6H_5CHOH \\ \quad | \\ C_6H_5CO \end{array} + HCOOH \rightarrow \begin{array}{l} C_6H_5CHOCHO \\ \quad | \\ C_6H_5CO \end{array}$$

$SOCl_2$ added portionwise with shaking to a mixture of benzoin and formic acid until the benzoin has dissolved → benzoin formate. Y: 91%. F. e. with PCl_3 s. H. Bredereck and R. Gompper, B. *87*, 726 (1954).

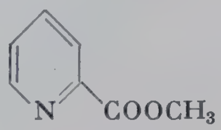
Thionyl chloride *$SOCl_2$*

Carboxylic acid esters from carboxylic acids COOH → COOR

s. *9*, 344

Thionyl chloride/sodium alkoxide *$SOCl_2/NaOR$*

263.



$SOCl_2$ added dropwise during 1 hr. with stirring to picolinic acid, refluxed 1 hr. with stirring, allowed to stand overnight, abs. methanol added to the rapidly stirred mixture, then a soln. of commercial 95%-Na-methoxide in methanol added slowly, and refluxed 30 min. with stirring → methyl picolinate. Y: 73.3-82%. R. Levine and J. K. Sneed, Am. Soc. *73*, 5614 (1951).

p-Toluenesulfonic acid *TsOH*

Ethers ROR

264. $S(CH_2CH_2OH)_2 + 2\ i\text{-}C_5H_{11}OH \rightarrow S(CH_2CH_2OC_5H_{11}\text{-}i)_2$

A mixture of thiodiglycol, 100%-excess isoamyl alcohol, and p-toluenesulfonic acid monohydrate refluxed 4 hrs. with stirring and separation of the water formed → bis-(2-isoamoxyethyl) sulfide. Y: 83%. F. e. s. F. Richter et al., Am. Soc. *74*, 4076 (1952).

Enolethers C:C(OR)

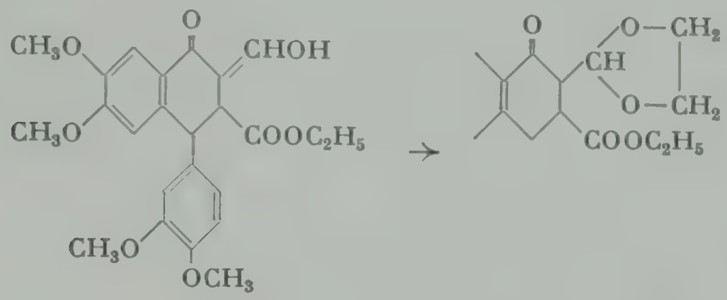
s. *6*, 215; s. a. A. Eschenmoser, J. Schreiber, and S. A. Julia, Helv. *36*, 482 (1953)

α,β-Ethyleneacetals from α,β-ethylenealdehydes $CHO \rightarrow CH(OR)_2$

265. $CH_2{=}CHCHO + 2\ HOC_2H_5 \rightarrow CH_2{=}CHCH(OC_2H_5)_2$

A soln. containing acrolein, abs. ethanol, Skellysolve F, and a trace of p-toluenesulfonic acid monohydrate refluxed 24 hrs. while the water formed is collected in a water separator → acrolein diethyl acetal. Y: 62.6-82%. D. I. Wisblat et al., Am. Soc. *75*, 5893 (1953).

α-Ketoacetals from α-hydroxymethyleneketones ←

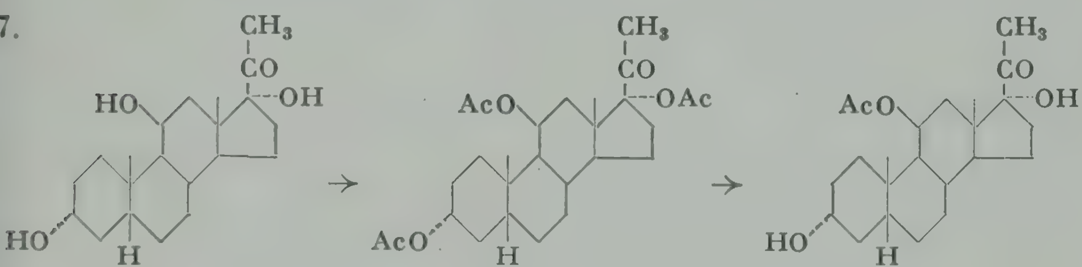
6. 

A soln. of 2-hydroxymethylene-3-carbethoxy-4-(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone, ethylene glycol, and p-toluenesulfonic acid in dry toluene refluxed 3 hrs. with separation of the water formed → ethylene acetal. Y: 51%. G. N. Walker, Am. Soc. *75*, 3393 (1953).

Blocking of keto groups by formation of alkylene ketals ←

s. *6*, 216; s. a. H. H. Inhoffen and J. Kath, B. *87*, 1589 (1954)

Acetylation Partial-O-deacetylation 11β-Acetoxysteroids ←

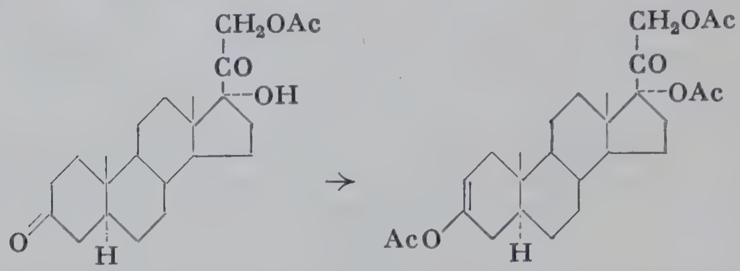
67. 

A small amount of p-toluenesulfonic acid added to a soln. of pregnan-3α,11β,17α-triol-20-one in acetic acid-acetic anhydride, the temp. maintained at ca. 25°, also during an exothermic reaction occurring after an induction period of 1-2 hrs., and the product isolated after standing overnight → pregnan-3α,11β,17α-triol-20-one triacetate (Crude Y: 98.4%) refluxed 24 hrs. with Na-carbonate in methanol-water → pregnan-3α,11β,17α-triol-20-one 11-acetate (Crude Y: 97%). E. P. Oliveto et al., Am. Soc. *75*, 5486 (1953).

Sulfosalicylic acid ←

Acetylation of alcohols with simultaneous formation of enolesters from ketones ←

268.



A mixture of acetic anhydride, toluene, and a little sulfosalicylic acid slowly distilled for ca. 45 min. until all acetic acid has been removed, 17α-hydroxy-21-acetoxyallopregnane-3,20-dione added, heated 3.5 hrs. with distillation of the resulting acetic acid, of which 1 mole is formed in 10 min., and a second mole in the next 2 hrs. → 3,17α,21-triacetoxy-2-allopregnen-20-one. Y: 84.4 %. (Am. Soc. *76*, 747.)—Sulfosalicylic acid is a stronger catalyst for enol acetylation than toluenesulfonic acid (Am. Soc. *76*, 743). F. e. s. H. V. Anderson et al., Am. Soc. *76*, 747, 743 (1954).

Sulfuric acid *H_2SO_4*

Alkoxyhalides from halogenhydrins ROR

269. $(C_6H_5)_2CHOH + HOCH_2CH_2Cl \rightarrow (C_6H_5)_2CHOCH_2CH_2Cl$

A mixture of ethylene chlorohydrin, concd. H_2SO_4, and benzene warmed on a water bath, a soln. of benzhydrol in benzene added during 30-50 min. with efficient stirring, and refluxed 4 hrs. with stirring → benzhydryl β-chloroethyl ether. Y: 81-88%. S. Sugasawa and K. Fujiwara, Org. Synth. *33*, 11 (1953).

α-Aminoalcohols from cyanohydrins with protection of the hydroxyl group by formation of alkoxymethyl ethers ←

270.

$$CH_3OCH_2CH(OH)CN + CH_2(OC_2H_5)_2 \rightarrow CH_3OCH_2CH(OCH_2OC_2H_5)CN$$

$$\downarrow$$

$$CH_3OCH_2CH(OH)CH_2NH_2 + CH_2(OC_2H_5)_2 \leftarrow CH_3OCH_2CH(OCH_2OC_2H_5)CH_2NH_2 + C_2H_5OH$$

3-Methoxy-2-hydroxypropionitrile, ethylal, and a little H_2SO_4 refluxed 0.5 hr. → 3-methoxy-2-ethoxymethoxypropionitrile (Y: 95%) hydrogenated 1 hr. with Raney-Ni in the presence of NH_3 at 108-125° and

450-700 atm. → 3-methoxy-2-ethoxymethoxypropylamine (Y: 90%) refluxed 15 min. with ethanol and HCl, then the ethanol-ethylal azeotrope and excess ethanol distilled off → 3-methoxy-2-hydroxypropylamine (Y: 88%). R. C. Schreyer, Am. Soc. *73*, 4404 (1951).

Ethylidene derivatives of carbohydrates $\begin{matrix} COH \\ | \\ COH \end{matrix} \rightarrow \begin{matrix} CO \\ | \\ CO \end{matrix} \!\!>\! C$

s. *9*, 355

Acetals from orthoformic acid esters $CO \rightarrow C(OR)_2$

s. *9*. 743; s. a. E. C. Kornfeld and R. G. Jones, J. Org. Chem. *19*, 1671 (1954)

Acetylation of quinols $OH \rightarrow OAc$

s. *1*, 181; also hydrolysis s. G. A. Reynolds and J. A. VanAllan, Org. Synth. *34*, 1 (1954)

Acoxy- from hydroxy-mercaptans $OH \rightarrow OAc$

1.

$$\begin{matrix} CH_2OH \\ | \\ CH_2SH \end{matrix} \rightarrow \begin{matrix} CH_2OCOCH_3 \\ | \\ CH_2SH \end{matrix}$$

Acetic anhydride added during 10 min. at ca. 40° to 2-mercaptoethanol containing acetic acid and a little H_2SO_4, warmed 1 hr. at 60°, then kept 20 hrs. at room temp. → 2-mercaptoethyl acetate. Y: 71%. L. W. C. Miles and L. N. Owen, Soc. *1952*, 817.

Carboxylic acid esters from carboxylic acids $COOH \rightarrow COOR$

s. *9*, 434

s. *5*, 172; s. a. O. Moldenhauer et al., A. *580*, 188 (1953)

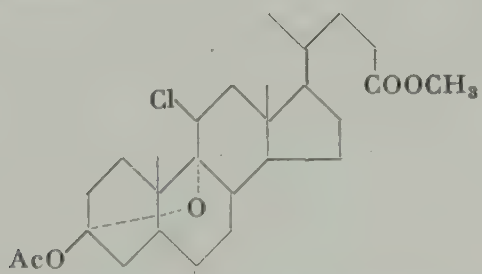
Perchloric acid $HClO_4$

Enolesters from ketones $CHCO \rightarrow C{:}C(OAc)$

s. *9*, 202

Lactolesters from lactols ←

2.



A cooled mixture of acetic anhydride and a little 70%-$HClO_4$ added to a soln. of methyl 3β-hydroxy-3α,9α-oxido-11β-chlorocholanate (prepn.

s. 596) in acetic acid and acetic anhydride, then allowed to stand 2 hrs. at room temp. → methyl 3β-acetoxy-3α,9α-oxido-11β-chlorocholanate. Y: 80%. F. e. with BF_3 s. H. Heymann and L. F. Fieser, Am. Soc. *73*, 5252 (1951).

Ammonium chloride *NH_4Cl*

Acetals from orthoformic acid esters $CO \rightarrow C(OR)_2$

s. *3*, 711; s. a. K. Balenović et al., J. Org. Chem. *18*, 297 (1953); method s. L. Claisen, B. *47*, 3171 (1914)

Hydrochloric acid *HCl*

Alkoxymethylureas from di(ureidomethyl) ethers ←

273. $(C_6H_5NHCONHCH_2)_2O + 2\ HOC_2H_5 \rightarrow 2\ C_6H_5NHCONHCH_2OC_2H_5$

Di-(3-phenylureidomethyl) ether shaken 10 min. at 25° with abs. ethanol containing HCl → 1-ethoxymethyl-3-phenylurea. Y: 90%. G. Zigeuner, M. *83*, 1099 (1952).

β-Ketoacetals from ketones via α-hydroxymethyleneketones ←

s. *9*, 816

Lactolides from lactols $OH \rightarrow OR$

s. *9*, 596

Acetylation of hydroxy compounds $OH \rightarrow OAc$

s. *9*, 791

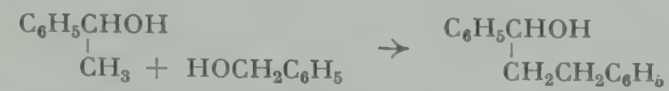
Carboxylic acid esters from carboxylic acids $COOH \rightarrow COOR$

274. $HOOC\cdot CH_2CH_2Si(CH_3)_2\cdot O\cdot Si(CH_3)_2\cdot CH_2CH_2COOH \rightarrow C_2H_5OOC\cdot CH_2CH_2Si(CH_3)_2\cdot O\cdot Si(CH_3)_2CH_2CH_2COOC_2H_5$

Siloxane derivatives. A mixture of 4,4,6,6-tetramethyl-4,6-disila-5-oxanonanedioic acid, abs. alcohol, and concd. HCl refluxed 18 hrs., then the water-alcohol azeotrope slowly distilled during 20 hrs. → diethyl 4,4,6,6-tetramethyl-4,6-disila-5-oxanonanedioate. Y: 90.2 %. L. H. Sommer and R. P. Pioch, Am. Soc. *75*, 6337 (1953). S. a. J. Bornstein, W. J. Reid, and D. J. Torres, Am. Soc. *76*, 2760 (1954).

Nickel-silica/potassium *Ni-SiO$_2$/K*

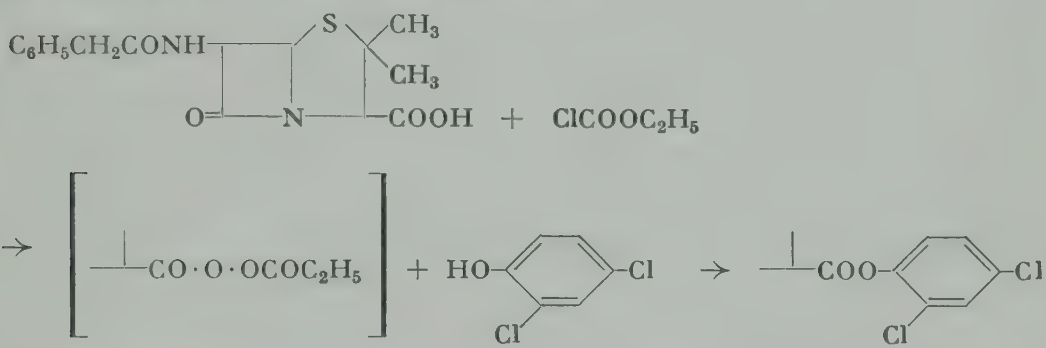
Disproportionative condensation
Modified Guerbet condensation ←

5. 

A mixture of α-methylbenzyl alcohol and benzyl alcohol, K, and U. O. P. nickel heated 11 min. at 184-207° → 1,3-diphenyl-1-propanol. Y: 84%. F. e., with lower rates and yields, s. E. F. Pratt and D. G. Kubler, Am. Soc. *76*, 52 (1954).

Via intermediates *v.i.*

Carboxylic acid esters
from carboxylic acids
via mixed alkoxyformic acid anhydrides COOH → COOR

76. 

Ethyl chloroformate added to an ice-cooled soln. of triethylammonium benzylpenicillinate in dry chloroform, after 10 min. 2,4-dichlorophenol and 5 drops of triethylamine added, kept 30 min. at 60° → 2,4-dichlorophenyl benzylpenicillinate. Y: 88%. F. e. s. R. L. Barnden et al., Soc. *1953*, 3733.

Nitrogen ↑ OC⇈N

Without additional reagents *w.a.r.*

Enolethers C:C(OH)

s. *4*, 215; s. a. A. Dornow and K. J. Fust, B. *87*, 985 (1954)

Carboxylic acid esters
from carboxylic acids COOH → COOR

s. *9*, 476

Orthocarboxylic acid esters
from iminoester hydrochlorides C(=NH)(OR) → C(OR)$_3$

s. *3*, 178; s. a. H. Stetter and K. H. Steinacker, B. *87*, 205 (1954)

Trialkyl- from dialkyl-oxonium salts ←
s. *9*, 990

Irradiation ←

Carboxylic acids from diazo oxides with ring contraction ←
s. *2*, 235; s. a. A. *579*, 133 (1953)

Sodium hydroxide *NaOH*

Aldehydes from nitrones
s. *9*, 553

$$CH{=}\overset{O}{\overset{\uparrow}{N}}R \rightarrow CHO$$

Degradation of peptides from the end bearing the free carboxyl group with carbodiimides via acylureas ←

277.

$$C_6H_5CONHCH_2CONHCH_2COOH + C\begin{matrix} \diagup NC_6H_4CH_3\text{-}p \\ \diagdown NC_6H_4CH_3\text{-}p \end{matrix}$$
$$\downarrow$$
$$C_6H_5CONHCH_2CONHCH_2CON\begin{matrix} \diagup CONHC_6H_4CH_3\text{-}p \\ \diagdown C_6H_4CH_3\text{-}p \end{matrix}$$
$$\downarrow$$
$$C_6H_5CONHCH_2COOH + \begin{matrix} NHCH_2CONHC_6H_4CH_3\text{-}p \\ | \\ CONHC_6H_4CH_3\text{-}p \end{matrix}$$

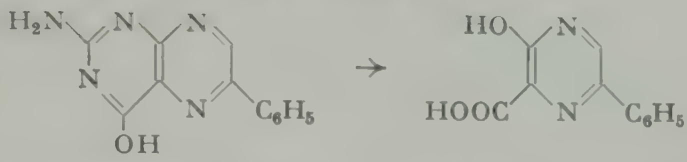
Di-p-tolylcarbodiimide added to a soln. of benzoylglycylglycine in warm anhydrous ethanol, and worked up after 24 hrs. at room temp. → 1-(benzoylglycylglycyl)-1,3-di-p-tolylurea (Y: 80%) dissolved in 75%-ethanol by warming, cooled rapidly, 0.1 *N* NaOH added with agitation, allowed to stand 10 min., neutralized with dil. HCl to pH 6, the solvent removed in vacuo, and treated with dil. aq. $NaHCO_3$-soln. → benzoylglycine (Y: 72%) and p-tolylcarbamylglycine p-toluidide (Y: 90%).—Although the method is effective in certain cases, the degraded peptides thus obtained tend to be contaminated with the startg. m. regenerated from the acylureas by simple hydrolysis. F. e. s. H. G. Khorana, Soc. *1952*, 2081.

Phenoxazines ○
s. *9*, 509

Pyrrolo(2′3′:3,4)isocoumarin ring opening
s. *9*, 740

Pyrimido[4,5-b]pyrazine ring opening

8.

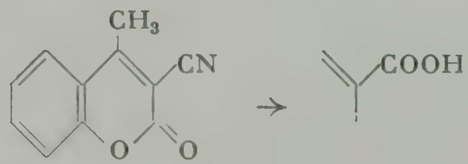


2-Amino-4-hydroxy-6-phenylpteridine in 4 *N* NaOH heated 24 hrs. at 170° in an autoclave → 2-hydroxy-5-phenylpyrazine-3-carboxylic acid. Y: 57%. F. e. s. F. E. King and P. C. Spensley, Soc. *1952*, 2144.

Sodium hydroxide/pyridine *NaOH/C_5H_5N*

Carboxylic acids from nitriles CN → COOH

79.



A mixture of 3-cyano-4-methylcoumarin (prepn. s. 814) and pyridine shaken with 4%-NaOH soln. at room temp. for 24 hrs. after complete soln. → 3-carboxy-4-methylcoumarin. Y: 78%.—The use of pyridine raised the yield from ca. 30% to 79%. C. H. Schroeder and K. P. Link, Am. Soc. *75*, 1886 (1953).

Potassium hydroxide *KOH*

Ethers from quaternary ammonium salts ←

s. *9*, 280

Oxo compounds from azomethines C:NR → CO

s. *9*, 857

Carboxylic acids from nitriles CN → COOH

s. *9*, 769, 866

Carboxythioethers from halogenonitriles

s. *9*, 691

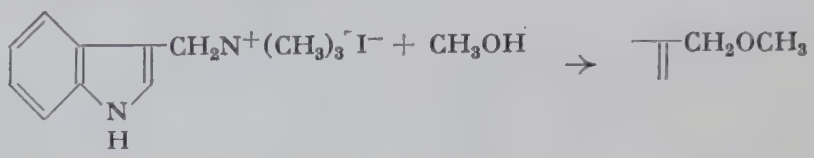
Sodium/alcohol *NaOR*

Replacement of nitro groups by alkoxyl NO_2 → OR

s. *8*, 235; s. a. C. K. Bradsher et al., Am. Soc. *74*, 4880 (1952); *76*, 2357 (1954)

Ethers from quaternary ammonium salts ←

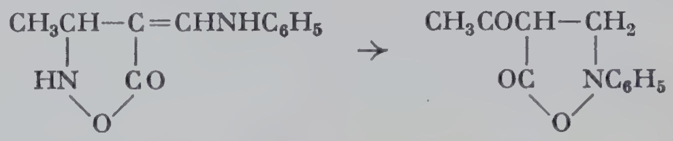
280.



Gramine methiodide added to a soln. of Na in methanol, then a N_2-stream passed through for 24 hrs. whereby trimethylamine is removed → 3-methoxymethylindole. Y: 79%. T. A. Geissman and A. Armen, Am. Soc. *74*, 3916 (1952); with KOH s. A. P. Terent'ev, A. N. Kost, and S. M. Gurvich, Ж. *23*, 615 (1953).

Rearrangement of isoxazolidones ←

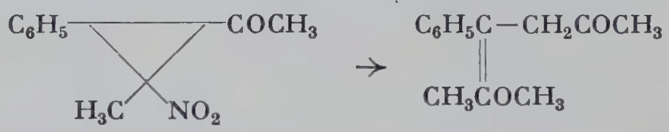
281.



2.2 g. 4-anilinomethylene-3-methylisoxazolid-5-one monohydrate in ethanol containing Na warmed 10 min. at 50° → 1 g. 4-acetyl-2-phenylisoxazolid-5-one. F. e. s. G. Shaw, Soc. *1952*, 3428.

Enolethers from nitrocyclopropanes C

282.



The solid stereoisomer of 3-phenyl-2-methyl-2-nitro-1-acetylcyclopropane in methanol added dropwise to a soln. of Na in methanol, and the product isolated after 10 min. → 5-methoxy-4-phenyl-4-hexene-2-one. Y: 98%.—The keto group is necessary for the reaction. L. I. Smith and J. S. Showell, J. Org. Chem. *17*, 827 (1952).

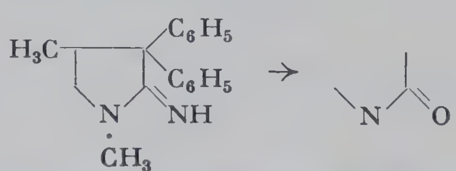
Sodium nitrite *$NaNO_2$*

Phenols from amines $NH_2 \rightarrow OH$

s. *3*, 183; s. a. H. Gies and E. Pfeil, A. *578*, 11 (1952)

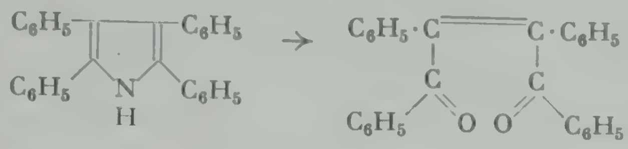
Replacement of imino groups by oxygen C:NH → CO

283.



2-Imino-1,4-dimethyl-3,3-diphenylpyrrolidine hydrochloride allowed to react with Na-nitrite and dil. HCl → 1,4-dimethyl-3,3-diphenylpyrrolidone. Y: ca. 100%. F. e. s. W. Wilson, Soc. *1952*, 3524.

Pyrrole ring opening



Satd. aq. $NaNO_2$ added portionwise with vigorous stirring at 80° to a mixture of tetraphenylpyrrole and glacial acetic acid, and stirring continued until a yellow soln. results → *cis*-dibenzoylstilbene. Y: 70%. R. Kuhn and H. Kainer, A. *578*, 227 (1952).

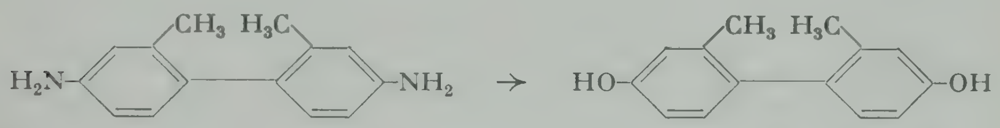
Sodium nitrite/trifluoroacetic acid — *$NaNO_2/CF_3COOH$*

Replacement of amino groups by hydroxyl — $NH_2 \rightarrow OH$

5. **Diazonium perhalogenocarboxylates.** Diazonium trifluoroacetates are comparatively stable. In aq. soln. they undergo smoothly and with good yields the usual replacement and coupling reactions.—E: Concd. aq. $NaNO_2$ added at 0-5° to aniline in ca. 1.5 *N* aq. trifluoroacetic acid until a slight excess is present, warmed 75 min. at 50°, then heated 15 min. at 100° → phenol. Y: 88%. F. e. and use of other perhalogenocarboxylic acids s. M. R. Pettit, M. Stacey, and J. C. Tatlow, Soc. *1953*, 3081.

Sodium nitrite/phosphoric acid — *$NaNO_2/H_3PO_4$*

6.



Phenols. 15 g. m-tolidine hydrochloride diazotized at 5° with $NaNO_2$ in aq. HCl, and the diazonium salt soln. boiled 10 min. with a large amount of dil. H_3PO_4 → 4,4′-dihydroxy-2,2′-dimethylbiphenyl. Y: 90%. H. Brockmann and A. Dorlars, B. *85*, 1168 (1952).

Cupric chloride — *$CuCl_2$*

α-Acoxyketones from α-diazoketones — $COCHN_2 \rightarrow COCH_2OAc$
α-Diazoketones as reagents for the identification of carboxylic acids

7.

The $CuCl_2$-catalyzed decomposition of α-diazoacetophenones in dioxane in the presence of a carboxylic acid yields phenacyl esters. Y: 60-100%. —E: p-Bromo-α-diazoacetophenone and propionic acid → p-bromophenacyl propionate. F. e. s. J. L. E. Erickson, J. M. Dechary, and M. R. Kesling, Am. Soc. *73*, 5301 (1951).

Barium hydroxide *$Ba(OH)_2$*

α-Aminocarboxylic acids
via hydantoins
s. *9*, 832

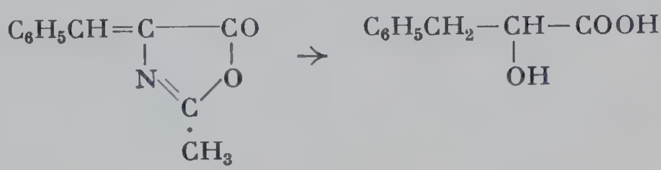
Zinc *Zn*

Ketones from α-nitroethylene derivatives $C:C(NO_2) \rightarrow CHCO$
s. *2*, 224; s. a. C. E. Anagnostopoulos and L. F. Fieser, Am. Soc. *76*, 532 (1954)

Zinc amalgam *Zn, Hg*

α-Hydroxycarboxylic acids from azlactones
Reductive oxazolone ring opening

288.

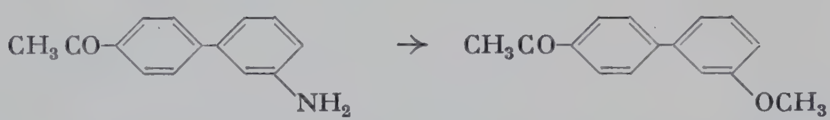


A mixture of 2-methyl-4-benzal-5-oxazolone, amalgamated Zn, and 6 *N* HCl refluxed 8 hrs. → phenyllactic acid. Y: good. E. C. Bubl and J. S. Butts, Am. Soc. *73*, 4972 (1951).

Zinc chloride *$ZnCl_2$*

Phenolethers and phenols ←
from amines
via diazonium chloride-zinc chloride complex

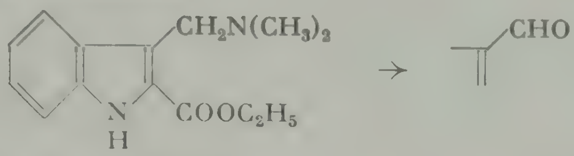
289.



3-Amino-4′-acetobiphenyl diazotized in aq. HCl with concd. aq. Na-nitrite at 0-5°, then $ZnCl_2$ added with stirring, the resulting diazonium chloride-zinc chloride complex isolated, the crude dry complex added to abs. methanol, and gently heated for 1 hr. until a test with an alkaline soln. of β-naphthol shows that the reaction is complete → 3-methoxy-4′-acetobiphenyl. Y: 68%.—Prepn. of phenols via the ethers using the above procedure may be recommended when the desired phenol is quite reactive and not sufficiently volatile with steam. F. e. s. C. K. Bradsher, F. C. Brown, and H. K. Porter, Am. Soc. *76*, 2357 (1954); method s. H. H. Hodgson and C. K. Foster, Soc. *1942*, 581.

Hexamethylenetetramine *$C_6H_{12}N_4$*

Aldehydes from tert. amines $CH_2NR_2 \rightarrow CHO$

0. 

Powdered hexamethylenetetramine added to a boiling soln. of 2-carbethoxy-3-dimethylaminomethylindole in glacial acetic acid, and refluxed 1 min. → 2-carbethoxyindole-3-aldehyde. Y: 68-72%.—Certain phenolic Mannich bases can be converted to aldehydes in the same way, but in poorer yields. Mannich bases derived from ketones evidently do not undergo the reaction. F. e. s. H. R. Snyder, S. Swaminathan, and H. J. Sims, Am. Soc. *74*, 5110 (1952).

Amino acid oxidase/catalase/oxygen ←

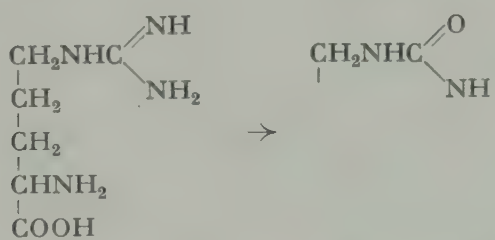
α-Ketocarboxylic acids from α-aminocarboxylic acids $CH(NH_2) \rightarrow CO$

1. $$(CH_3)_2CHCH_2\underset{NH_2}{CH}COOH \rightarrow (CH_3)_2CHCH_2COCOONa$$

Catalase and L-amino acid oxidase soln. added successively to an aq. suspension of L-leucine, kept at 37° and pH 7.2 (adjusted by addition of 2 *N* NaOH) in an O_2-stream, with occasional addition of caprylic alcohol to control foaming, until the oxidation is complete, then the product isolated as the Na-salt → Na-α-ketoisocaproate. Y: 70-85%. F. e., also from D-amino acids with D-amino acid oxidase, s. A. Meister, Biochem. Prep. *3*, 66 (1953).

Streptococcus faecalis ←

Ureas from guanidines $NHC(:NH)NH_2 \rightarrow NHC(:O)NH_2$

2. 

A cell suspension of Streptococcus faecalis treated with cetyltrimethylammonium bromide, then added to a soln. of L-arginine monohydrochloride and Na-acetate in dil. acetic acid, incubated at 37° until after ca. 1 hr. all the arginine has disappeared, and the product isolated as the Cu-chelate → Cu-L-citrulline. Y: 90%. V. A. Knivett, Biochem. Prep. *3*, 104 (1953).

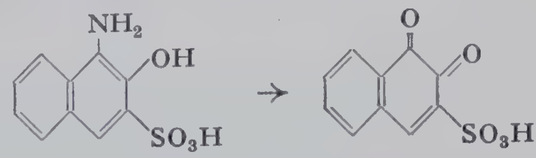
Trifluoroacetic acid/sodium nitrite — *$CF_3COOH/NaNO_2$*

s. Sodium nitrite/trifluoroacetic acid

Nitric acid/ether — *$HNO_3/(C_2H_5)_2O$*

Quinones from aminophenols ←

293.



1-Amino-2-naphthol-3-sulfonic acid added to an ice-cold soln. of concd. HNO_3 in ether (caution!), and the product isolated after 1-3 hrs. → 1,2-naphthoquinone-3-sulfonic acid. Y: almost 100%. F. e. s. W. Langenbeck, H. Le Blanc, and B. Lukowczyk, B. *87*, 496 (1954).

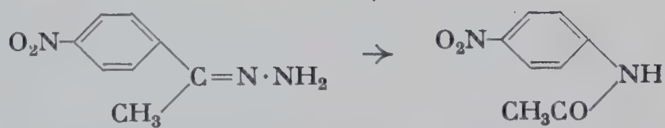
Phosphoric acid/sodium nitrite — *$H_3PO_4/NaNO_2$*

s. Sodium nitrite/phosphoric acid

Nitrosyl sulfate — *$ONOSO_3H$*

Subst. carboxylic acid amides from hydrazones and semicarbazones by rearrangement ←

294.

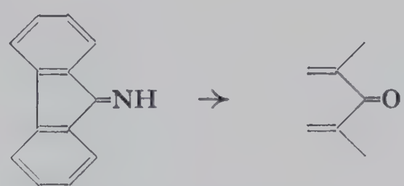


p-Nitroacetophenone hydrazone added portionwise during 45 min. below 15° to a well-stirred soln. of nitrosyl sulfate (from $NaNO_2$ and 90%-H_2SO_4), and the product isolated when the foaming has subsided → p-nitroacetanilide. Y: 75%. F. e., also rearrangement of semicarbazones and stereoisomers, s. D. E. Pearson, K. N. Carter, and C. M. Greer, Am. Soc. *75*, 5905 (1953).

Sulfuric acid — *H_2SO_4*

Ketones from imines — C:NH → CO

295.

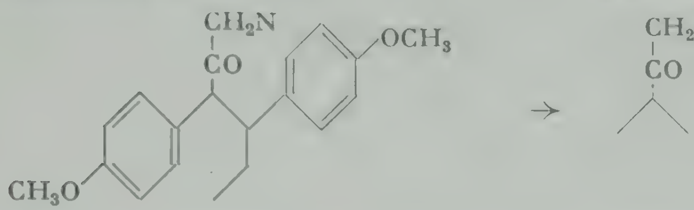


1.0 g. 9-iminofluorene refluxed 30 min. with 30%-H_2SO_4 → 0.87 g. fluorenone. C. L. Arcus and R. J. Mesley, Soc. *1953*, 178.

Oxo compounds from acylhydrazones — C:N·NHAc → CO

s. *9*, 431

α-Hydroxyketones from α-diazoketones $COCHN_2 \rightarrow COCH_2OH$



A mixture of 1-diazo-3,4-bis-(p-methoxyphenyl)-2-hexanone, dioxane, and 2 *N* H_2SO_4 warmed 0.5 hr. at 60-65° → 1-hydroxy-3,4-bis-(p-methoxyphenyl)-2-hexanone. Y: 82%. J. H. Burckhalter and J. Sam, Am. Soc. *74*, 187 (1952).

Sulfuric acid/acetic acid *H_2SO_4/CH_3COOH*

Carboxylic acids from nitriles $CN \rightarrow COOH$

o-Chlorophenylacetonitrile refluxed ca. 1 hr. with a mixture of equal volumes concd. H_2SO_4, glacial acetic acid, and water → o-chlorophenylacetic acid. Y: 89%. F. e. s. G. S. Misra and J. S. Shukla, J. Indian Chem. Soc. *28*, 480 (1951).

Hydrochloric acid *HCl*

Replacement of amino groups by hydroxyl $NH_2 \rightarrow OH$

s. *2*, 233; s. a. C. F. Koelsch and N. F. Albertson, Am. Soc. *75*, 2095 (1953)

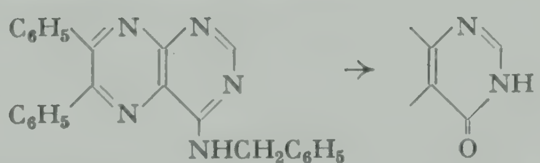
Oxo compounds from azomethines $C{:}NR \rightarrow CO$

s. *9*, 730

Ketones from enamines $CH{:}C{\cdot}N\langle \rightarrow CH_2CO$

s. *7*, 217; s. a. G. Shaw and G. Sugowdz, Soc. *1954*, 665

Replacement of amino groups by oxygen ←



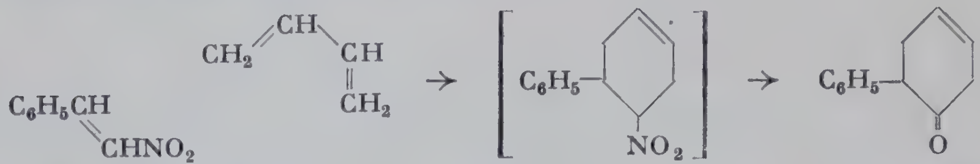
A soln. of 4-benzylamino-6,7-diphenylpteridine in 6 *N* HCl refluxed 0.5 hr. → 6,7-diphenyl-4(3H)-pteridinone. Y: 93%. F. e. s. E. C. Taylor, Jr., J. A. Carbon, and D. R. Hoff, Am. Soc. *75*, 1904 (1953).

Carboxylactones from cyanolactones CN → COOH

s. *9*, 826

Cyclohexenones via nitrocyclohexenes ←

Diene synthesis followed by Nef reaction

299. 

A mixture of β-nitrostyrene, butadiene, toluene, and a trace of hydroquinone heated 48 hrs. at 100° in a sealed tube → 4-nitro-5-phenylcyclohexene (Y: 88%) in ethanol treated with a soln. of 2 equivalents of Na in ethanol, allowed to stand 1 hr. under N_2, then added dropwise at 0° under N_2 to a well-stirred mixture of HCl, water, and ethanol, stirring continued 1 hr. at 0°, then at room temp. until the color changes from green to yellow → 6-phenyl-3-cyclohexen-1-one (Y: 76-78%). F. e. s. W. C. and R. B. Wildman, J. Org. Chem. *17*, 581 (1952); cf. E. E. van Tamelen and R. J. Thiede, Am. Soc. *74*, 2615 (1952).

Hydantoins from α-ureidonitriles ○

s. *9*, 245

300. 

1-Subst. hydantoins. HCl added to a soln. of N-cyclohexyl-N-carbamidoglycinonitrile in ethanol, whereupon the product separates after a short time → 1-cyclohexylhydantoin. Y: 90%. E. S. Rothman and A. R. Day, Am. Soc. *76*, 111 (1954).

Halogen ↑ OC ⇅ Hal

Without additional reagents *w.a.r.*

Bromohydrins from 1,2-dibromides CBrCBr → C(OH)CBr

s. *9*, 307

Aminoethers from aminoalcohols Hal → OR

301. $(C_6H_5)_2C(COOH)\cdot Br + HOCH_2CH_2NHCH_3 \rightarrow (C_6H_5)_2C(COOH)\cdot O\cdot CH_2CH_2NHCH_3,HBr$

A soln. of β-methylaminoethanol in benzene added during 1 hr. to a soln. of 1 molar equivalent of α-bromo-α,α-diphenylacetic acid in the same solvent, and refluxed 8 hrs. → α-(β-methylaminoethoxy)-α,α-diphenylacetic acid hydrobromide. Y: 73.5%. H. S. Mosher, M. B. Frankel, and M. Gregory, Am. Soc. *75*, 5326 (1953).

Carboxylic acid esters
from carboxylic acid chlorides COCl → COOR

s. 2. 277; phenol esters s. J. Colonge and R. Chambard, Bl. *1953*, 573

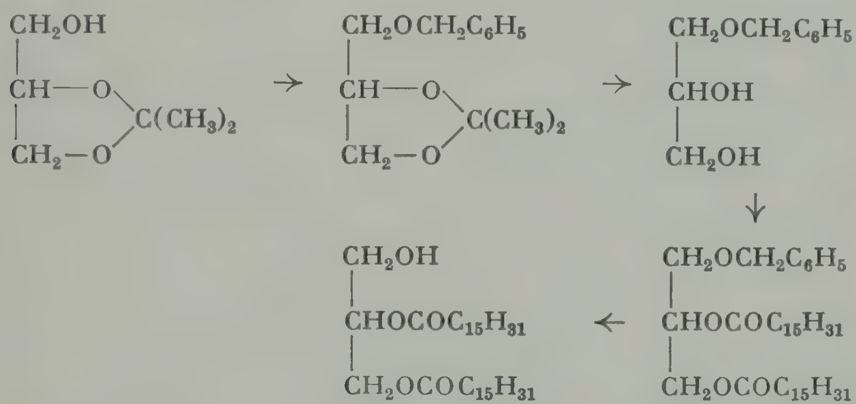
Reactions with fluoro compounds ←
Carboxylic acid amides
from 1,1,1-dihalogenamines

$$CHClFCF_2N(C_2H_5)_2 \rightarrow CHClFCON(C_2H_5)_2$$

Polyfluoroalkyl-*tert*-amines are highly reactive in contrast to the corresponding ethers, sulfides, and sulfones (Am. Soc. *74*, 749).—E: N-(2-Chloro-1,1,2-trifluoroethyl)diethylamine stirred with excess water → N,N-diethyl-α-chloro-α-fluoroacetamide. Y: ca. 100%. R. L. Pruett et al., Am. Soc. *72*, 3646 (1950); reaction with alcohols s. Am. Soc. *74*, 749 (1952).

Sodium *Na*

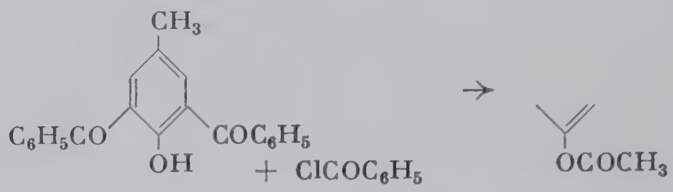
1,2-Diglycerides Hal → OR
Blocking of hydroxyl groups
by formation of benzyl ethers
Cleavage of acetals



1,2-Isopropylideneglycerol added portionwise with stirring to powdered Na in toluene, refluxed 1 hr. after the vigorous reaction has subsided, ca. 1 molar equivalent benzyl chloride added to the gently refluxing stirred soln. during 0.5 hr., and heating continued for 1 hr. → 3-benzyl-1,2-isopropylideneglycerol (Y: 78%) heated 2 hrs. with 10%-acetic acid on a boiling water bath with frequent shaking → 1-benzylglycerol (Y: 87%) and pyridine dissolved in CCl_4, treated with palmitoyl chloride in CCl_4, and kept overnight at 40° → 3-benzyl-1,2-dipalmitoylglycerol (Y: 88%) dissolved with gentle warming in n-hexane, and hydrogenated 2 hrs. with Pd-black until the H_2-uptake has ceased → 1,2-dipalmitin (Y: 93%). F. e. s. R. J. How and T. Malkin, Soc. *1951*, 2663.

O-Acylation OH → OAc

304.



A soln. of 2,6-dibenzoyl-p-cresol in dry benzene treated during 2 hrs. with small pieces of Na with occasional shaking and gentle heating towards the end of the reaction, separated from excess Na, then treated dropwise with acetyl chloride until decolorized → 2,6-dibenzoyl-p-cresol acetate. Y: 99.7%.—Acetylation in the usual way was unsuccessful. M. S. Newman and A. G. Pinkus, J. Org. Chem. *19*, 992 (1954).

Potassium *K*

Carbalkoxyenolethers ←
from β-ketocarboxylic acid esters

s. *6*, 243; cf. S. J. Rhoads, R. D. Reynolds, and R. Raulins, Am. Soc. *74*, 2889 (1952)

Sodium hydride *NaH*

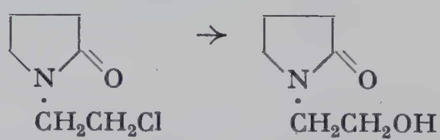
Ethers from halides Hal → OR

s. *5*, 194; methoxylation s. C. D. Hurd and W. H. Saunders, Jr., Am. Soc. *74*, 5324 (1952)

Sodium hydroxide *NaOH*

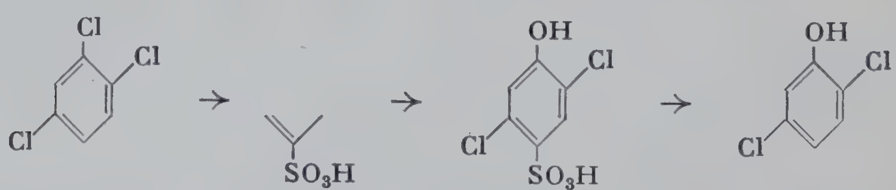
Replacement of chlorine by hydroxyl Cl → OH

305.



A suspension of finely powdered NaOH in benzene added to N-(β-chloroethyl)-2-pyrrolidone, and refluxed 12 hrs. → N-(β-hydroxyethyl)-2-pyrrolidone. Y: 76%. B. Puetzer, L. Katz, and L. Horwitz, Am. Soc. *74*, 4959 (1952).

306.



via sulfonic acids. Crude 1,2,4-trichlorobenzene (prepn. s. 973) added with stirring during 10 min. to 25%-oleum, and the product isolated as the Na-salt after several min. more → crude Na-2,4,5-trichlorobenzenesulfonate (Y: 93-95%) heated 2 hrs. with aq. NaOH at 230° and

150-160 lb. pressure → Na-2,5-dichloro-4-phenolsulfonate (Y: 86-87%) gently boiled with 70%-H_2SO_4 for 2 hrs. → 2,5-dichlorophenol (Y: 71-73.5%). A. Galat, Am. Soc. *74*, 3890 (1952).

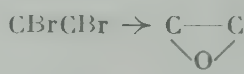
Halogenethers from dihalides Hal → OR

s. *9*, 312

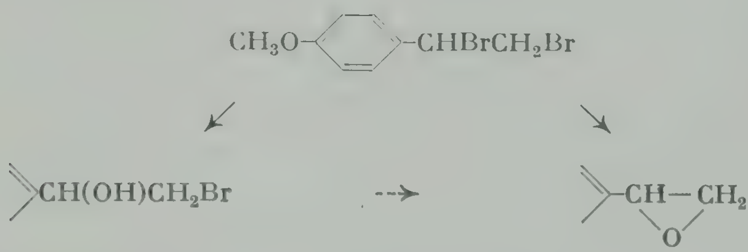
Acyl peroxides from carboxylic acid chlorides 2 RCOCl → $(RCOO)_2$

s. 5, 95; s. a. J. d'Ans, J. Mattner, and W. Busse, Ang. Ch. *65*, 57 (1953)

Oxido compounds and bromohydrins from 1,2-dibromides



7.



p-Methoxystyrene dibromide dissolved in dioxane, an equal volume

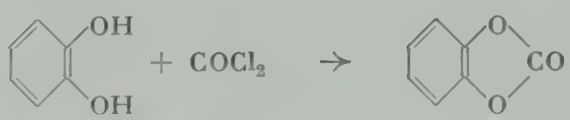
water added in one portion with stirring, and the product isolated after 2-3 min. when the turbid mixture has become clear → p-methoxystyrene bromohydrin. Y: 87-100%.

aq. NaOH added in one portion with stirring at room temp., and the product isolated after 10-15 min. → p-methoxystyrene oxide. Y: 86.6%.

C. O. Guss, Am. Soc. *74*, 2561 (1952); cf. Am. Soc. *75*, 3177 (1953).

Carbonic acid esters ←

8.

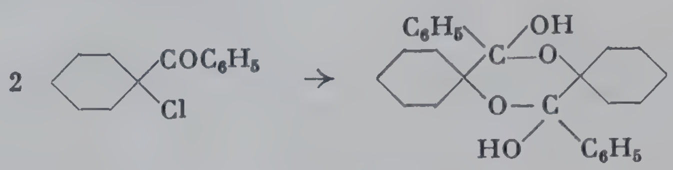


A soln. of commercial $COCl_2$ in toluene added at 0-5° portionwise with efficient stirring during 60-75 min. to a soln. of catechol in deaerated aq. NaOH under N_2, stirring continued 1 hr. at 0-5°, then allowed to come to room temp. → o-phenylene carbonate. Y: 79-86%. R. S. Hanslick, W. F. Bruce, and A. Mascitti, Org. Synth. *33*, 74 (1953).

Potassium hydroxide *KOH*

p-Dioxanes by dimerization

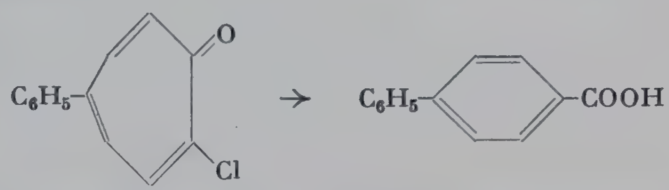
309.



A soln. of 10 g. 1-chlorocyclohexyl phenyl ketone in anhydrous ether stirred 24 hrs. in the presence of fused KOH → 8 g. 1-hydroxycyclohexyl phenyl ketone dimer (startg. m. f. 796). I. Elphimoff-Felkin and B. Tchoubar, Bl. *1952*, 551.

Carboxylic acids from cyclic α-halogenoketones Ring contraction ←

310.

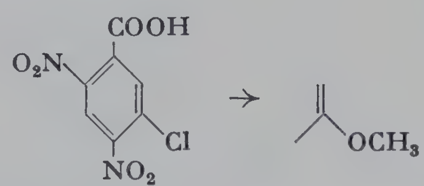


Benzene ring from tropone ring. A mixture of 2-chloro-5-phenyltropone and 10% alc. KOH refluxed 10 min. on a steam bath → diphenyl-4-carboxylic acid. Y: 97%. F. e. s. W. von E. Doering and L. H. Knox, Am. Soc. *75*, 297 (1953).

Potassium hydroxide/alcohol

Ethers from halides Hal → OR

311.



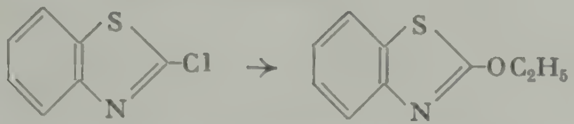
A soln. of 4,6-dinitro-3-chlorobenzoic acid in methanol added to a soln. of KOH in abs. methanol, and allowed to stand 12 hrs. at room temp. → 4,6-dinitro-3-methoxybenzoic acid. Y: 77%. H. Goldstein and R. Stamm, Helv. *35*, 1330 (1952); α-alkoxyacetylene derivatives s. A. N. Pudovik, Ж. *21*, 1462 (1951); C. A. *46*, 4467 b.

Halogenethers from dihalides

312. 4 moles pentamethylene dibromide, 1 mole guaiacol, and methanolic 2.7 *N* KOH heated 2 hrs. on a steam bath → 5-o-methoxyphenoxypentyl bromide (startg. m. f. 888). Y: 76%. F. e. s. A. W. Nineham, Soc. *1953*, 2601; with aq. NaOH, added slowly, s. P. A. Boivin et al., Can. J. Chem. *30*, 994 (1952); cf. Can. J. Chem. *30*, 592.

Sodium/alcohol *NaOR*

Replacement of chlorine by alkoxyl



2-Chlorobenzothiazole added dropwise during 10 min. at 0° to a soln. of the equivalent amount of Na in abs. ethanol, then refluxed 30 min. → 2-ethoxybenzothiazole (startg. m. f. 20). Y: 93%.—Excess Na-ethoxide lowers the yield. F. e. s. H. Gilman, K. E. Lentz, and J. A. Beel, Am. Soc. *74*, 1081 (1952).

Simultaneous
O- and C-methylation
s. *9*, 882

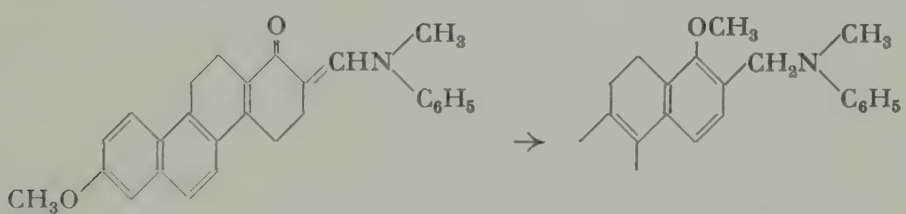
Carboxylic acid esters
from α-halogenoketones ←

$$(C_6H_5)_2CClCOCH_3 \rightarrow (C_6H_5)_2CHCH_2COOC_2H_5$$

A soln. of Na in ethanol added to a soln. of α-chloro-α,α-diphenylacetone (prepn. s. 626) in abs. ethanol, and the product isolated after a few min. → ethyl β,β-diphenylpropionate. Y: 85%. C. L. Stevens and A. E. Sherr, J. Org. Chem. *17*, 1228 (1952).

Potassium/alcohol *KOR*

Aromatization of
α-aminomethyleneketones ←



0.75 g. 1,2,3,4,5,6-hexahydro-3-keto-10-methoxy-4-N-methylanilinomethylenechrysene in tetrahydrofuran added to a soln. of K in *tert*-butanol under N_2, refluxed 5 min., and methyl iodide added to the boiling soln. to discharge the brown color → 0.52 g. 1,2-dihydro-3,10-dimethoxy-4-N-methylanilinomethylchrysene. A. J. Birch, J. A. K. Quartey, and H. Smith, Soc. *1952*, 1768.

Sodium carbonate *Na_2CO_3*

Replacement of bromine by hydroxyl Br → OH

s. *3*, 207; s. a. R. Grewe, W. Lorenzen, and L. Vining, B. *87*, 793 (1954)

Potassium carbonate *K_2CO_3*

Alkoxymethylene- from hydroxymethylene compounds C:CHOH → C:CHOR

s. *4*, 775; s. a. E. Ott and D. S. Tarbell, Am. Soc. *74*, 6266 (1952)

Potassium hydrogen carbonate *$KHCO_3$*

Replacement of halogen by acoxy groups Hal → OAc

s. *9*, 642

Sodium formate *HCOONa*

Replacement of halogen by hydroxyl Hal → OH

replacement of bromine s. *6*, 249; of chlorine s. C. D. Hurd and K. L. Kreuz, Am. Soc. *74*, 2965 (1952)

Potassium acetate *CH_3COOK*

Replacement of bromine by acoxy groups in silanes, also cleavage Br → OAc

316. $(CH_3)_3SiCH(Br)C_6H_5 \rightarrow (CH_3)_3SiCH(OCOCH_3)C_6H_5$ $+ CH_3COOK$ $(CH_3)_3SiC(Br)(C_6H_5)_2 \rightarrow HC(OCOCH_3)(C_6H_5)_3$

α-Bromobenzyltrimethylsilane	Diphenyl-α-bromomethyltrimethylsilane
refluxed with K-acetate in glacial acetic acid	
for 18-24 hrs., then allowed to stand 24-36 hrs. longer → α-trimethylsilylbenzyl acetate. Y: 84%.	for 7.5 hrs. → benzhydryl acetate. Y: 79%.

F. e. s. C. R. Hauser and C. R. Hance, Am. Soc. *74*, 5091 (1952).

Potassium oxalate *$(COOK)_2$*

Aldehydes from 1,1-dibromides $CHBr_2 \rightarrow CHO$

s. *7*, 292; s. a. J. C. Bill and D. S. Tarbell, Org. Synth. *34*, 82 (1954)

Sodium salt *Na^+*

Arylethers ArOR

s. *9*, 953

Carboxylic acid anhydrides from carboxylic acid chlorides RCO·O·OCR′

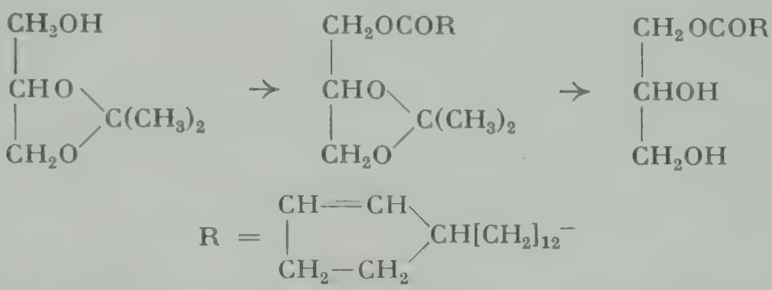
317. $C_6H_5CH_2COCl + NaOOC\cdot CH_2C_6H_5 \rightarrow C_6H_5CH_2\cdot CO\cdot O\cdot OC\cdot CH_2C_6H_5$

1 molar equivalent of phenylacetic chloride added dropwise to a stirred suspension of 1 molar equivalent of Na-phenylacetate in ben-

zene, and stirring continued for 3 hrs. → phenylacetic anhydride. Y: 87%. F. e. s. J. A. King and F. H. McMillan, Am. Soc. *73*, 4911 (1951).

Pyridine C_5H_5N

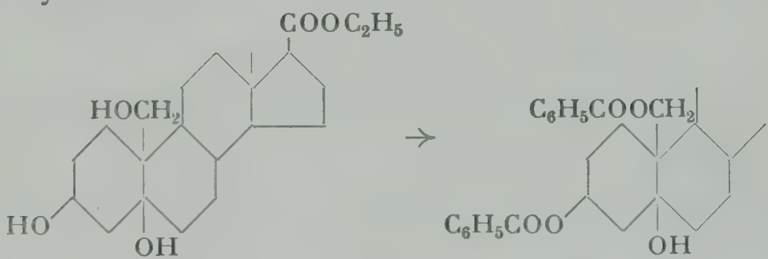
Glycerides OH → OAc
Cleavage of acetals

8. 

Chaulmoogroyl chloride added with shaking to isopropylideneglycerol and dry pyridine in benzene, and allowed to stand overnight → isopropylideneglycerol chaulmoograte (Y: 83%) in ether cooled in an ice-bath, treated slowly with ice-cold concd. HCl with vigorous shaking and kept 0.5 hr. in the ice-bath with frequent shaking → 1-monochaulmoogrin (Y: 90%). F. e., also di- and tri-glycerides, s. A. Gupta and T. Malkin, Soc. *1952*, 2405.

1,2-Diglycerides
s. *9*, 303

Selective acylation

9. 

Benzoyl chloride added at -10^0 to ethyl 3β,5,19-trihydroxyetiocholanate in pyridine, and kept overnight at room temp. → ethyl 3β,19-dibenzoxy-5-hydroxyetiocholanate. Y: 86%. P. T. Herzig and M. Ehrenstein, J. Org. Chem. *17*, 713 (1952).

O-Carbethoxylation OH → $OCOOC_2H_5$

0. cf. Synth. Meth. *7*, 301
Equatorial hydroxyl groups at C_6, C_7, C_{12}, and C_{17} of steroids are invariably carbethoxylated while polar hydroxyl groups are not. Activation by a double bond overcomes hindrance effects. Carbethoxylation also in dioxane in the presence of pyridine s. L. F. Fieser et al., Am. Soc. *74*, 3309 (1952).

Carboxylic acid anhydrides from carboxylic acid chlorides and carboxylic acids $RCOCl + HOOCR \rightarrow RCO \cdot O \cdot OCR$

321. $n\text{-}C_6H_{13}COCl + HOOC \cdot C_6H_{13}\text{-}n \rightarrow C_6H_{13} \cdot CO \cdot O \cdot OC \cdot C_6H_{13}$

n-Heptanoyl chloride added at -10^0 to an ethereal soln. of n-heptanoic acid and pyridine → n-heptanoic anhydride. Y: 97%. W. Gerrard and A. M. Thrush, Soc. *1953*, 2117.

Urethans from phenols $OH \rightarrow OCONR_2$

s. *3*, 216; s. a. H. Gilman et al., J. Org. Chem. *19*, 1067 (1954)

Copper *Cu*

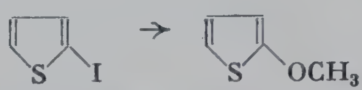
Diaryl ethers $Ar \cdot O \cdot Ar$

Ullmann reaction

s. *2*, 255; *4*, 240; s. a. W. M. Whaley, L. Starker, and M. Meadow, J. Org. Chem. *18*, 833 (1953)

Cupric oxide *CuO*

Ethers from halides $Hal \rightarrow OR$

322. 

2-Iodothiophene and pulverized CuO added to a soln. of Na in abs. methanol, and gently refluxed 30 hrs. with stirring → 2-methoxythiophene. Y: 80%.—Cupric oxide is more satisfactory than cuprous oxide or copper. J. Sicé, Am. Soc. *75*, 3697 (1953).

Silver oxide Ag_2O

Methylation of carbohydrates $OH \rightarrow OR$

s. *2*, 257/8; s. a. P. J. Stoffyn and R. W. Jeanloz, Am. Soc. *74*, 563 (1954)

Silver carbonate Ag_2CO_3

Replacement of bromine by hydroxyl $Br \rightarrow OH$

Carbohydrates

s. *3*, 218; s. a. H. G. Fletcher, Jr., Am. Soc. *75*, 2624 (1953)

Silver nitrate $AgNO_3$

Nitric acid esters from halides $Hal \rightarrow ONO_2$

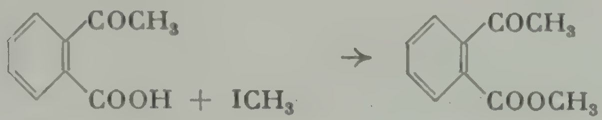
323. $C_2H_5OOC \cdot CH_2CH_2Br \rightarrow C_2H_5OOC \cdot CH_2CH_2ONO_2$

The use of Ag-nitrate in acetonitrile is a very convenient method for preparing laboratory quantities of pure nitrates. The reaction may be followed by weighing the Ag-halide precipitate.—E: A soln. of ethyl β-bromopropionate in acetonitrile added to a soln. of Ag-nitrate in acetonitrile, and allowed to stand 3 days at room temp. → ethyl hydracrylate nitrate. Y: 58%. F. e. s. A. F. Ferris et al., Am. Soc. *75*, 4078 (1953).

Silver salt *Ag⁺*

Carboxylic acid esters COOR

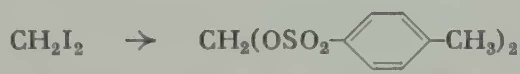
4.



A threefold excess of methyl iodide added dropwise to crude Ag-o-acetobenzoate (prepared from a soln. of a-acetobenzoic acid in 2 *N* NaOH and $AgNO_3$), and worked up after cooling to room temp. → methyl o-acetobenzoate. Y: 88%.—By this procedure, formation of the pseudoester is avoided. J. H. Boyer and D. Straw, Am. Soc. *75*, 2683 (1953).

Sulfonic acid esters ←

5.



A soln. of Ag-p-toluenesulfonate and methylene iodide in *acetonitrile* refluxed 24 hrs. → methylene bis-tosylate. Y: 87%. F. e. s. W. D. Emmons and A. F. Ferris, Am. Soc. *75*, 2257 (1953).

Calcium chloride $CaCl_2$

Acetals from 1,1-acoxyhalides C(OAc)Hal → $C(OR)_2$
s. *9*, 600

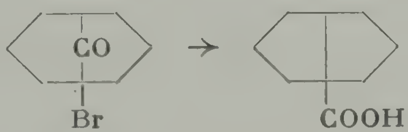
Magnesium oxide *MgO*

Carboxylic acids from carboxylic acid chlorides COCl → COOH
s. *9*, 402

Mercuric acetate $(CH_3COO)_2Hg$

Carboxylic acids from cyclic α-halogenoketones Ring contraction ←

26.



Mercuric acetate and 1-bromobicyclo[3.3.1]nonan-9-one added to dry *tert*-butanol, refluxed 6 hrs., filtered from traces of a solid, and poured into water → bicyclo[3.3.0]octane-1-carboxylic acid. Y: 74%. A. C. Cope and E. S. Graham, Am. Soc. *73*, 4702 (1951).

Aluminum halides $AlHal_3$

Acylation of unreactive alcohols OH → OAc
s. *8*, 286; s. a. Am. Soc. *76*, 2329 (1954)

Formamide *$HCONH_2$*

Reaction of halides with formamide ←
Hydrolysis of halides
α-Hydroxy- from α-halogeno-carboxylic acid esters
Carboxylic acids from 1,1,1-trihalides

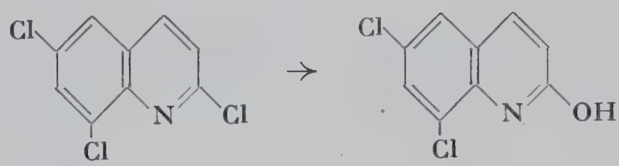
327. $$C_2H_5\underset{Br}{CH}COOC_2H_5 \rightarrow C_2H_5\underset{OH}{CH}COOC_2H_5$$

Ethyl α-bromobutyrate allowed to react with formamide and the theoretical amount of water at 150° for 5 hrs. with vigorous stirring → ethyl α-hydroxybutyrate. Y: 91%.—Similarly at 100°: Benzotrichloride → benzoic acid. Y: 80%.—Also formoxy compounds and carboxylic acid amides in the absence of water s. H. Bredereck, R. Gompper, and G. Theilig, B. *87*, 537 (1954).

Sulfuric acid *H_2SO_4*

Partial replacement of halogen by hydroxyl Hal → OH

328.



A mixture of 2,6,8-trichloroquinoline and H_2SO_4-water heated 3.5 hrs. in an oil bath at 170-210° → 6,8-dichloro-2-hydroxyquinoline. Y: almost 100%. F. e. s. C. R. Saunders, C. E. Smith, Jr., and J. D. Capps, Am. Soc. *73*, 5910 (1951).

Selective formation of carboxylic acids from 1,1,1-trichlorides $CCl_3 \rightarrow COOH$

329. $$CF_3CH{=}CHCCl_3 \rightarrow CF_3CH{=}CHCOOH$$

1,1,1-Trichloro-4,4,4-trifluoro-2-butene (prepn. s. 132) heated with concd. H_2SO_4 → γ,γ,γ-trifluorocrotonic acid. Y: 68%. R. N. Haszeldine, Soc. *1953*, 922.

Hydrochloric acid *HCl*

Aminoalcohols from acylaminohalides ←

330. $$ClCH_2\underset{C_6H_5}{\underset{|}{C}}HNHCOCH_3 \rightarrow HOCH_2\underset{C_6H_5}{\underset{|}{C}}HNH_2$$

N-(2-Chloro-1-phenylethyl)acetamide heated 24 hrs. with concd. HCl on a steam bath → β-hydroxy-α-phenylethylamine hydrochloride. Y: 90%. F. e. s. T. L. Cairns et al., J. Org. Chem. *17*, 751 (1952).

Sulfur ↑ OC⇅S

Without additional reagents *w.a.r.*

Ethers from tosylates OTs → OR

s. 5, 207; also in the presence of H_2SO_4 s. M. N. Huffman and J. W. Sadler, J. Org. Chem. *18*, 919 (1953)

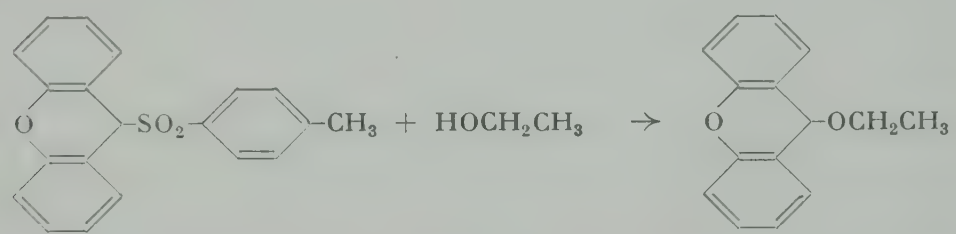
Alkali hydroxide ←

Replacement of sulfonic acid groups by hydroxyl $SO_3H \rightarrow OH$

s. 2, 268; *3*, 229; s. a. C. F. Koelsch and N. F. Albertson, Am. Soc. *75*, 2095 (1953); comparison of NaOH and KOH s. S. W. Englund, R. S. Aries, and D. F. Othmer, Ind. Eng. Chem. *45*, 189 (1953)

Potassium hydroxide *KOH*

Ethers from sulfones $SO_2R \rightarrow OR'$



p-Tolyl xanthhydryl sulfone refluxed 4 hrs. with a *N* soln. of KOH in 80%-ethanol → ethyl xanthhydryl ether. Y: 74%. F. e. s. M. P. Balfe, J. Kenyon, and E. M. Thain, Soc. *1952*, 790.

Sodium/alcohol *NaOR*

Ethers ROR

s. *9*, 800

Potassium carbonate *K_2CO_3*

in toluene s. *2*, 271; in nitrobenzene s. G. Wolf, Am. Soc. *75*, 2673 (1953)

Sodium acetate *CH_3COONa*

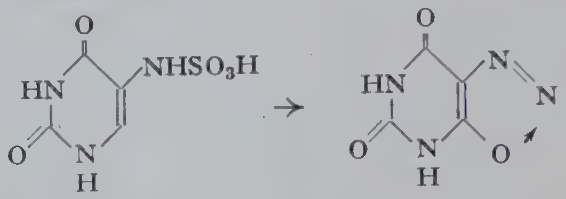
Acetoxy compounds from p-toluenesulfonic acid esters OTs → OAc

s. *6*, 263; s. a. W. A. Bonner and C. J. Collins, Am. Soc. *75*, 5372 (1953)

Nitric acid/sodium nitrite *$HNO_3/NaNO_2$*

Diazo oxides from sulfamic acids ←

332.



8.3 g. 5-sulfaminouracil (prepn. s. 675) in 40 c.c. HNO_3 (d. 1.40) heated a short time until reaction sets in and a soln. is obtained, then concentrated in vacuo → 5-diazobarbituric acid. Y: 90%. Also with less HNO_3 in the presence of $NaNO_2$ to start the reaction s. F. G. Fischer, W. P. Neumann, and J. Roch, B. 85, 752 (1952).

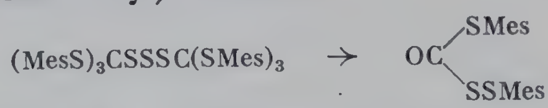
Phosphorus/hydriodic acid *P/HI*

s. Hydriodic acid/phosphorus

Hydrogen peroxide *H_2O_2*

Aryltrithiopercarbonic acid esters from bis(triarylthiomethyl) trisulfides ←

333.

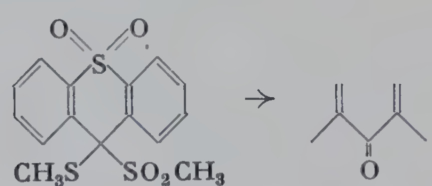


5 molar equivalents 33%-H_2O_2 added to a soln. of bis(trimesitylthiomethyl) trisulfide in acetic acid, then evaporated → dimesityl trithiopercarbonate. Y: 71%. F. e. s. H. J. Backer and E. Westerhuis, R. 71, 1071 (1952).

Hydrochloric acid *HCl*

Cleavage of sulfonylthioethers ←

334.



10-(Methylthio)-10-(methylsulfonyl)thiaxanthene 5,5-dioxide refluxed 1 hr. with acetic acid and concd. HCl → 10-thiaxanthenone 5,5-dioxide. Y: 90%. H. Kloosterziel, W. van der Veen, and H. J. Backer, R. 71, 1231 (1952).

Acetals from sulfurous acid esters $CO \rightarrow C(OR)_2$

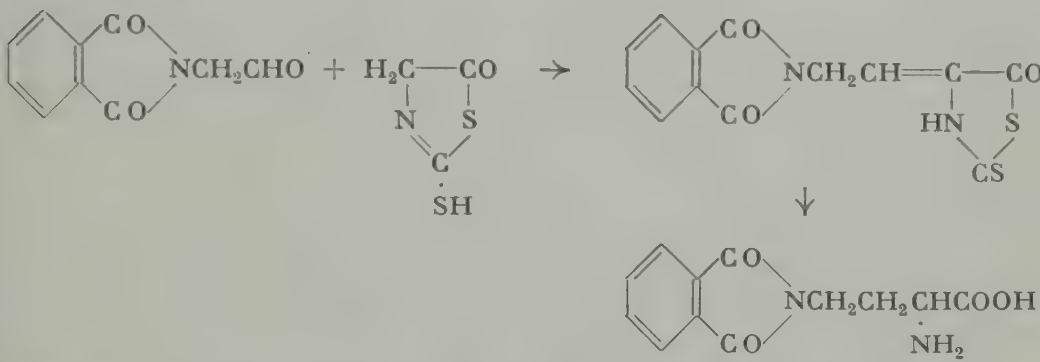
335. $C_6H_5CH{=}CBrCHO + (CH_3O)_2SO \rightarrow C_6H_5CH{=}CBrCH(OCH_3)_2$

A mixture of α-bromocinnamaldehyde, dimethyl sulfite, and abs. methanol containing HCl refluxed 8-10 hrs. at a bath temp. of 120-130° until

the SO_2-evolution ceases → α-bromocinnamaldehyde dimethyl acetal. Y: 91%. F. e. s. F. Wille and F. Knörr, B. *85*, 841 (1952); method s. W. Voss and E. Blanke, A. *485*, 258 (1931).

Hydriodic acid/phosphorus *HI/P*

α-Aminocarboxylic acids from aldehydes via 5-thiazolidone-2-thiones Synthesis with addition of 2 C-atoms ←

6. 

Phthalimidoacetaldehyde and 2 drops of piperidine added to a soln. of 2-mercapto-5-thiazolone in hot acetic acid, and allowed to stand 24 hrs. at room temp. → 2-thio-4-(phthalimidoethylidene)thiazolid-5-one (Y: 92%) cleaved with red P and HI (s. Synth. Meth. *6*, 269) → α-amino-γ-phthalimidobutyric acid (Y: 90%). F. e. s. K. Balenović, I. Jambrešić, and I. Furić, J. Org. Chem. *17*, 1459 (1952).

Remaining Elements ↑ OC ⇅ Rem

Without additional reagents *w.a.r.*

Hydroperoxides from Grignard reagents R·MgHal → R·OOH

37. $(CH_3)_3C \cdot MgCl + O_2 \rightarrow [(CH_3)_3C \cdot OOMgCl] \rightarrow C \cdot (CH_3)_3C \cdot OOH$

Ethereal *tert*-butyl-MgCl added during 40 min. at −71° to O_2-satd. ether → *tert*-butyl hydroperoxide. Y: 85.7% (by titration). F. e. s. C. Walling and S. A. Buckler, Am. Soc. *75*, 4372 (1953).

Carbon ↑ OC ⇅ C

Without additional reagents *w.a.r.*

Transesterification COOR → COOR′

s. *7*, 312; s. a. A. Nickon and L. F. Fieser, Am. Soc. *74*, 5566 (1952)

38. $(C_2H_5O)_4Ti + 4\ n\text{-}C_6H_{13}OH \rightarrow (n\text{-}C_6H_{13}O)_4Ti + 4\ C_2H_5OH$

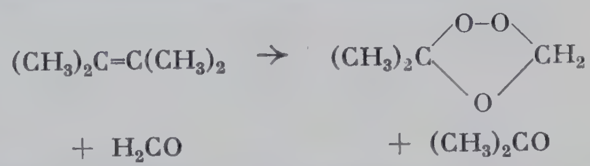
Titanic acid esters. Ethyl orthotitanate and n-hexanol heated until distillation of ethanol ceases → n-hexyl orthotitanate. Y: 85.9%. F. e., also from $TiCl_4$, s. B. A. Arbuzov and Z. G. Isaeva, Ж. *22*, 566 (1952); C. A. *47*, 2684 f.

339. $$(C_2H_5O)_2P\cdot OH + n\text{-}C_4H_9OH \rightarrow \begin{matrix} C_2H_5O \diagdown \\ \quad P\cdot OH \\ n\text{-}C_4H_9O \diagup \end{matrix}$$

Mixed dialkyl phosphites. A mixture of diethyl phosphite and n-butanol slowly heated up to a bath temp. of 150°, when a brisk reaction starts, kept 55 min. at 150-155° with distillation of ethanol, then distilled under reduced pressure → ethyl butyl phosphite. Y: 45%. F. e. s. G. M. Kosolapoff, Am. Soc. *73*, 4989 (1951).

1,2,4-Trioxolanes from ethylene derivatives ○

340.



Tetramethylethylene added to formaldehyde in liq. methyl chloride, then ozonized with 6%-O_3 at −80° until a blue color persists → isobutylene ozonide. Y: 55%. F. e. s. R. Criegee, G. Blust, and H. Zinke, B. *87*, 766 (1954).

Potassium hydroxide/alcohol *KOH*

Hydrolytic cleavage of the carbon chain ←

s. *9*, 797

Sodium/alcohol *NaOR*

Partial transesterification COOR → COOR

341. $$H_2C\begin{matrix} \diagup COOC_2H_5 \\ \diagdown COOC_2H_5 \end{matrix} \rightarrow C_6H_5CH_2OH \rightarrow H_2C\begin{matrix} \diagup COOC_2H_5 \\ \diagdown COOCH_2C_6H_5 \end{matrix}$$

A mixture of 2 moles diethyl malonate, 1 mole benzyl alcohol, and benzene distilled slowly through a Fenske column until any water present is removed, after slight cooling Na-ethoxide in ethanol added, benzene-ethanol azeotrope then distilled off until interchange is complete → benzyl ethyl malonate. Y: 74%.—The use of less malonic ester gives more dibenzyl ester but causes no difficulty in isolation of the product. R. E. Bowman and W. D. Fordham, Soc. *1951*, 2753.

Ammonia *NH_3*

Degradation of carbohydrates with loss of 1 C-atom via mercaptals and 1,1-disulfones ←

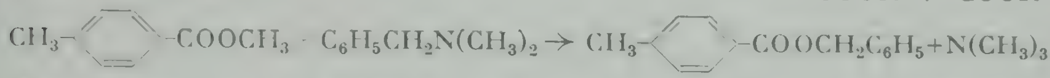
342. cf. Synth. Meth. *7*, 324.

The procedure has been improved and simplified by oxidizing the unacetylated rather than the acetylated mercaptals with perpropionic acid

instead of monoperphthalic acid and performing the degradation of the resulting 1.1-disulfones with very dil. aq. NH_3. D. L. MacDonald and H. O. L. Fischer, Biochem. et Biophys. Acta *12*, 203 (1953).

Benzyldimethylamine *$C_6H_5CH_2N(CH_3)_2$*

Transesterification COOR → COOR′

3. 

Methyl p-toluate and 33% excess benzyldimethylamine heated 23 hrs. at 170-210° under a slow stream of N_2 until the evolution of trimethylamine ceases → benzyl p-toluate. Y: 96%; conversion 82%. F. e. s. E. L. Eliel and R. P. Anderson, Am. Soc. *74*, 547 (1952).

Fehling solution ←

Aldehydes from hydrobenzoins ArCH(OH)CH(OH)Ar → 2 ArCHO
s. *9*, 732

Barium hydroxide/oxygen s. Oxygen/barium hydroxide *$Ba(OH)_2/O_2$*

Aluminum alkoxide *$Al(OR)_3$*

Transesterification COOR → COOR′
Optically active
α-aminocarboxylic acid esters
Carboxylic acid esters from carboxylic acids

4. $(CH_3)_2CHCH_2CH(NH_2)COOH$ (L) → $(CH_3)_2CHCH_2CH(NH_2)COOCH_3$ (L) + HOC_6H_{13}–n → $(CH_3)_2CHCH_2CH(NH_2)COOC_6H_{13}$–n (L)

$SOCl_2$ added dropwise below −5° to methanol, then L-leucine added portionwise at the same temp., warmed slowly to 40°, and stirring continued for 2 hrs. → L-leucine methyl ester (Y: 83-86%) added to a soln. of Al-isopropoxide in abs. n-hexanol, warmed 45-50 min. at 55° and 55-60 min. at 65° in a dry, CO_2-free stream of air at 14 mm. → L-leucine n-hexyl ester (Y: 71-72%).—Racemization takes place, when Na-alkoxide is used as a catalyst. M. Brenner and W. Huber, Helv. *36*, 1109 (1953).

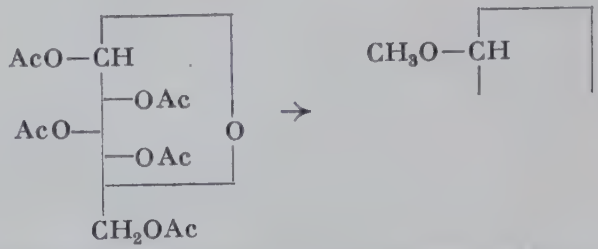
Nitrobenzene *$C_6H_5NO_2$*

Oxidative cleavage ←
of ethylene derivatives
s. *4*, 259; *7*, 321; s. a. I. A. Pearl and D. L. Beyer, Am. Soc. *74*, 4263 (1952)

Stannic chloride *$SnCl_4$*

Glycosides OAc → OR

345.

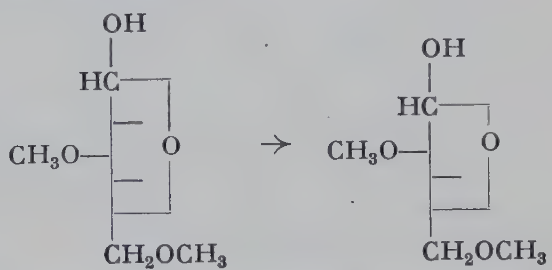


β-Glucopyranosides. A soln. of $SnCl_4$ in benzene added at 40° to a soln. of pentaacetyl-β-D-glucopyranose in benzene containing dry methanol, and the product isolated after 1 hr. at the same temp. → methyl tetraacetyl-β-D-glucopyranoside. Y: 53-57%. Also phenyl analog s. R. U. Lemieux and W. P. Shyluk, Can. J. Chem. *31*, 528 (1953).

Lead tetraacetate *$(CH_3COO)_4Pb$*

Degradation of carbohydrates ←

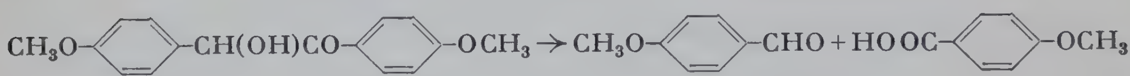
346.



A soln. of Pb-tetraacetate in glacial acetic acid added with cooling at 20° to a soln. of 2,6-dimethyl-D-glucose in glacial acetic acid, kept 10 min. at room temp., and the resulting 4-formyl-2,5-dimethyl-D-arabinose deformylated by heating in aq. 0.5 *N* HCl on a steam bath for 45 min. → 2,5-dimethyl-D-arabinose. Y: ca. 100%. J. Fried and D. E. Walz, Am. Soc. *74*, 5468 (1952); s. a. A. S. Perlin, Am. Soc. *76*, 2595 (1954).

Oxidative cleavage of α-hydroxyketones and α-ketocarboxylic acids
α-Diketones from α-hydroxyketones

347. $C_6H_5COCOOH + C_2H_5OH \rightarrow C_6H_5COOC_2H_5$



$C_6H_5CH(OH)COC_6H_5 \rightarrow C_6H_5COCOC_6H_5$

Pb-tetraacetate effects quantitative oxidate cleaveage of α-hydroxyketones and α-ketocarboxylic acids, in the presence of substances forming pseudoglycols by addition (e.g. water, alcohols, HCN). In their absence, no reaction takes place between Pb-tetraacetate and α-ketocarboxylic acids, whereas α-hydroxyketones are oxidized without cleavage to the respective α-diketones in good yield. Esters in place

of the acids are obtained as degradation products in the presence of alcohols.—E: A soln. of Pb-tetraacetate in benzene added to a soln. of phenylglyoxylic acid in dry benzene-ethanol, and kept 1 hr. at 45° → ethyl benzoate. Y: 80%.—Finely powdered Pb-tetraacetate added to a soln. of anisoin in 90%-acetic acid, kept 20 min. at 50-55° with frequent shaking, then Pb^{++} precipitated as Pb-sulfate by addition of the calculated amount of concd. H_2SO_4 → anisic acid (Y: 76.8%) and anisaldehyde (Y: 83% as the p-nitrophenylhydrazone).—Finely powdered Pb-tetraacetate added to a soln. of benzoin in glacial acetic acid, and kept 24 hrs. at 50° with occasional shaking → benzil. Y: 83.4%. F. e. s. E. Baer, Am. Soc. *62*, 1597 (1940); cleavage of α-hydroxyketones s. a. D. Y. Curtin and S. Leskowitz, Am. Soc. *73*, 2633 (1951); cleavage of α-ketocarboxylic acids s. a. W. Voser et al., Helv. *35*, 2414 (1952).

Sodium bismuthate *$NaBiO_3$*

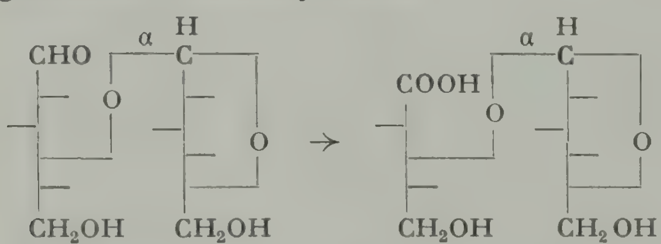
Oxidative degradation ←

s. *6*, 277; steroid derivatives s. F. Ungar and R. I. Dorfman, Am. Soc. *76*, 1197 (1954)

Oxygen/barium hydroxide *$O_2/Ba(OH)_2$*

Spengler and Pfannenstiel oxidative degradation of carbohydrates COOH

8.



An aq. soln. of 18 g. maltose added with agitation during 2-3 hrs. to aq. $Ba(OH)_2$ under O_2, and the product isolated after 24-25 hrs. → 17 g. crude 3-[α-D-glucosido]-D-arabonic acid. F. e. s. E. Hardegger. K. Kreis, and H. El Khadem, Helv. *35*, 618 (1952).

Ozone/zinc *O_3/Zn*

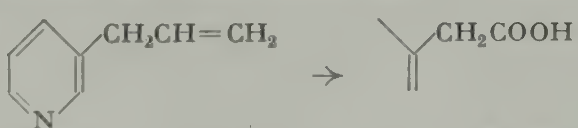
Oxo compounds from ethylene derivatives CO

s. *6*, 280; s. a. A. F. Daglish, J. Green, and V. D. Poole, Soc. *1954*, 2627

Ozone/hydrogen peroxide *O_3/H_2O_2*

Carboxylic acids from ethylene derivatives COOH

9.

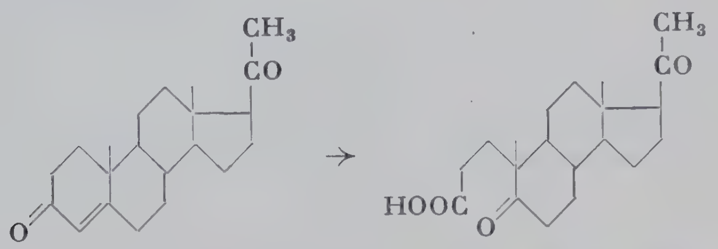


A slow stream of O_3 passed through a soln. of 3-allylpyridine in aq. HCl with water-cooling until after 45 min. the theoretical amount of

O_3 has been taken up, then 30%-H_2O_2 added to complete the oxidation of the aldehydes formed by ozonolysis to carboxylic acids, and allowed to stand overnight at room temp. → 3-pyridineacetic acid hydrochloride. Y: almost 100%. J. P. Wibaut and H. C. Beyerman, R. *70*, 977 (1951).

Oxidative ring opening C

350.

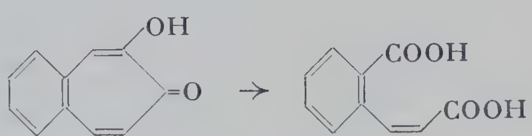


A soln. of progesterone in 5:4 ethyl acetate-glacial acetic acid ozonized by passing through it 3 molar equivalents of O_3 at a rate of 150 ml./min., 30%-H_2O_2 added, and placed in the refrigerator overnight → 5,20-diketo-3,5-seco-A-norpregnan-3-oic acid. Y: 79%. G. I. Fujimoto and J. Prager, Am. Soc. *75*, 3259 (1953); s. a. M. Gut, Helv. *36*, 906 (1953); F. L. Weisenborn, D. C. Remy, and T. L. Jacobs, Am. Soc. *76*, 552 (1954).

Hydrogen peroxide/potassium hydroxide *H_2O_2/KOH*

Oxidative tropolone ring opening

351.



A soln. of 0.4 g. 4,5-benzotropolone and H_2O_2 in aq. KOH kept 12 hrs. at 50°, then allowed to stand 14 days at room temp. → 0.2 g. o-carboxycinnamic acid. H. Fernholz, E. Hartwig, and J.-C. Salfeld, A. *576*, 131 (1952).

p-Toluenesulfonic acid *TsOH*

Acoxy compounds from ethers OR → OAc

s. *4*, 262; s. a. J. Org. Chem. *18*, 919 (1953)

Enol acetates from ketones ←

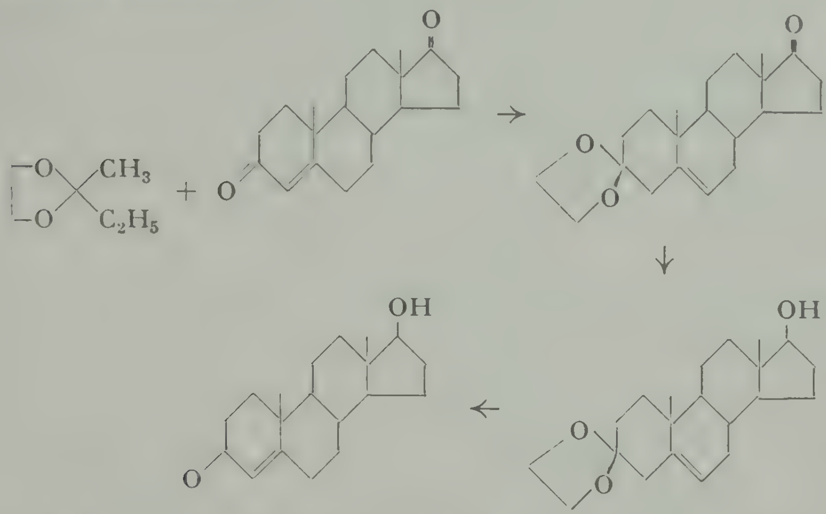
s. *8*, 307; s. a. C. Djerassi and C. T. Lenk, Am. Soc. *76*, 1722 (1954)

β-Ketocarboxylic acid esters from 6-keto-1,3-diox-4-enes C

s. *9*, 212

Transdioxolanation ←
Protection of keto groups
Alcohols from ketones

2.

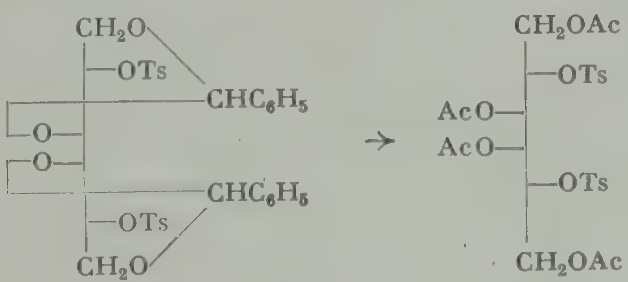


A soln. of Δ^4-androstene-3,17-dione and a little p-toluenesulfonic acid monohydrate in 2-methyl-2-ethyl-1,3-dioxolane distilled slowly through a glass helices-packed column over a period of 5.5 hrs. → 3-ethylenedioxy-Δ^5-androsten-17-one (Y: 74%) in abs. ethanol added to prehydrogenated W-4 Raney-Ni (cf. Synth. Meth. 7, 39) in ethanol, hydrogenated at atmospheric pressure until after 1 hr. 1 equivalent of H_2 has been absorbed, filtered, 2-methyl-2-ethyl-1,3-dioxolane added, and concentrated under reduced pressure to remove the ethanol → 3-ethylenedioxy-Δ^5-androsten-17α-ol (Y: 90%) dissolved in anhydrous acetone, a little p-toluenesulfonic acid monohydrate added, and refluxed 14 hrs. → crude testosterone (Y: ca. 100%). Over-all Y: 67%.—The same yield was obtained when the reduction was carried out by $LiAlH_4$ in tetrahydrofuran.—Transdioxolanation appears to be more subject to steric and electronic effects than direct dioxolanation, the reactivity order found with steroids being: satd. 3- and 20-ketones $\rangle$ α,β-unsatd. 3- and 20-ketones $\rangle$ 2- or 4-monobromo-3-ketones $\rangle\rangle$ (no reaction) 17-ketones, 2,4-dibromo-3-ketones. F. transdioxolanations s. H. J. Dauben, Jr., B. Löken, and H. J. Ringold, Am. Soc. 76, 1359 (1954).

Sulfuric acid H_2SO_4

Acoxy compounds from acetals ←

53.



1,3:4,6-Dibenzylidene-2,5-ditosyldulcitol, acetic anhydride, acetic acid, and concd. H_2SO_4 heated 1 hr. on a steam bath until all the solid has been dissolved → 1,3,4,6-tetraacetyl-2,5-ditosyldulcitol. Y: 78%. N. K. Matheson and S. J. Angyal, Soc. *1952*, 1133.

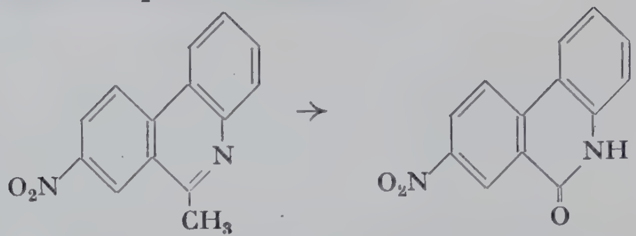
Enol acetates from ketones ←

s. *8*, 307; s. a. W. R. Vaughan and K. M. Milton, Am. Soc. *74*, 5623 (1952); N. S. Leeds, D. K. Fukushima, and T. F. Gallagher, Am. Soc. *76*, 2943 (1954)

Chromic acid *CrO_3*

Phenanthridones from phenanthridines ←

354.



1 g. 6-methyl-8-nitrophenanthridine, Na-dichromate, and acetic acid refluxed 2 hrs. → 0.85 g. 8-nitrophenanthridone. A. J. Nunn, K. Schofield, and R. S. Theobald, Soc. *1952*, 2797.

Periodic acid *HIO_4*

Oxidative degradation of side chains ←

s. *1*, 240; s. a. R. Hirschmann et al., Am. Soc. *76*, 4013 (1954); cleavage of α-hydroxyketones s. G. W. Stacy and R. A. Mikulec, Am. Soc. *76*, 524 (1954)

Osmium tetroxide *OsO_4*

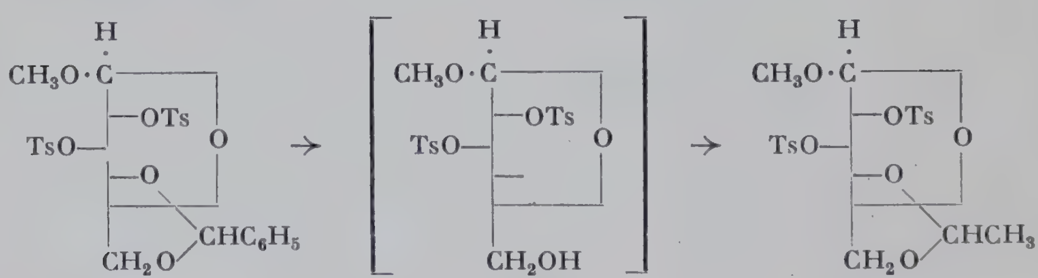
α-Hydroxyketones from α,β-ethylenenitriles C:C(CN) → C(OH)CO
17α-Hydroxy-20-ketosteroids

s. *4*, 268; s. a. Huang-Minlon, R. Tull, and J. Babcock, Am. Soc. *76*, 2396 (1954); R. E. Jones and F. W. Kocher, Am. Soc. *76*, 3682 (1954)

Via intermediates *v.i.*

Transacetalization ←
Ethylidene from benzylidene derivatives of carbohydrates

355.



A soln. of α-methyl 4,6-benzylidene-2,3-ditosyl-D-glucoside in acetone-water containing HCl left 8 days at room temp. until the optical rotation is constant, neutralized with K-carbonate, acetone evaporated, the residue extracted with chloroform, shaken with $NaHSO_3$-soln. to remove benzaldehyde, dried, evaporated, and the residue shaken 48 hrs. with paraldehyde containing concd. H_2SO_4 → α-methyl 4,6-ethylidene-2,3-ditosyl-D-glucoside. Y: 77%. E. G. Ansell and J. Honeyman, Soc. *1952*, 2778.

Elimination

Hydrogen ↑ OC⇑H

Silver oxide/magnesium sulfate *$Ag_2O/MgSO_4$*

Quinones from quinols ←

s. *9*, 256

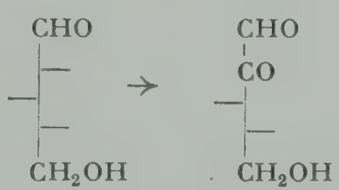
Cupric hydroxide/acetic acid *$Cu(OH)_2/CH_3COOH$*

Benzils from hydrobenzoins CH(OH)CH(OH) → COCO

s. *9*, 732

Cupric acetate *$(CH_3COO)_2Cu$*

Osones from carbohydrates CH(OH)CO → COCO



Methanol and cupric acetate added to an aq. soln. of D-xylose, quickly brought to the boil, and refluxed 10 min. → crude D-xylosone. Y: 50-55%. J. K. Hamilton and F. Smith, Am. Soc. *74*, 5162 (1952); s. a. L. L. Salomon, J. J. Burns, and C. G. King, Am. Soc. *74*, 5161 (1952).

Aluminum alkoxide *$Al(OR)_3$*

Ketones from sec. alcohols with simultaneous migration of the carbon carbon double bond CHOH → CO

with Al-isopropoxide s. *2*, 286; also with isobutyl methyl ketone in the absence of an inert solvent s. A. F. Daglish, J. Green, and V. D. Poole, Soc. *1954*, 2627; with Al-*tert*-butoxide s. F. Johnson, G. T. Newbold, and F. S. Spring, Soc. *1954*, 1302

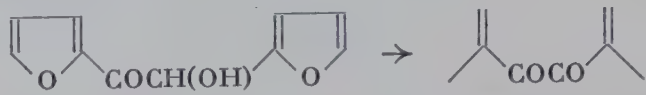
Thallous alkoxide *TlOR*

Benzils from benzoins

357. 

Excess thallous ethoxide in benzene added to a soln. of anisoin in benzene → anisil. Y: 91%.—Aliphatic acyloins are not oxidized by a similar treatment. F. e. s. L. P. McHatton and M. J. Soulal, Soc. *1952*, 2771.

Thallous alkoxide/nitrobenzene *$TlOR/C_6H_5NO_2$*

358. 

A small quantity of a satd. soln. of thallous ethoxide in ethanol added to a mixture of furoin and nitrobenzene in abs. ethanol, and the product isolated after 24 hrs. → furil. Y: 83%. F. e. s. L. P. McHatton and M. J. Soulal, Soc. *1953*, 4095.

N-Bromoacetamide *$CH_3CONHBr$*

Ketones from sec. alcohols CH(OH) → CO

s. *7*, 333; *8*, 323; s. a. A. R. Hanze et al., Am. Soc. *76*, 3179 (1954)

Lead tetraacetate *$(CH_3COO)_4Pb$*

α-Diketones from α-hydroxyketones

s. *9*, 347

α-Keto- from α-hydroxy-carboxylic acid esters CH(OH)COOR → COCOOR

359. $C_6H_5CH(OH)COO$–(–)menthyl → C_6H_5COCOO–(–)menthyl

A soln. of (–)menthyl D,L-mandelate in abs. benzene refluxed 8 hrs. with the theoretical amount of finely powdered Pb-tetraacetate, with occasional shaking → (–)menthyl phenylglyoxylate (startg. m. f. 741). Y: 85%. F. e. s. V. Prelog and H. L. Meier, Helv. *36*, 320 (1953).

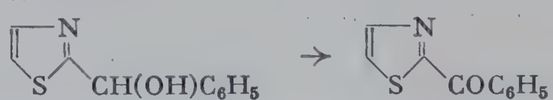
Nitrogen oxides ←

Quinones from quinols ←

s. *1*, 161; s. a. A. G. Brook, Soc. *1952*, 5040

Sodium dichromate/acetic acid *$Na_2Cr_2O_7/CH_3COOH$*

Ketones from sec. alcohols CHOH → CO

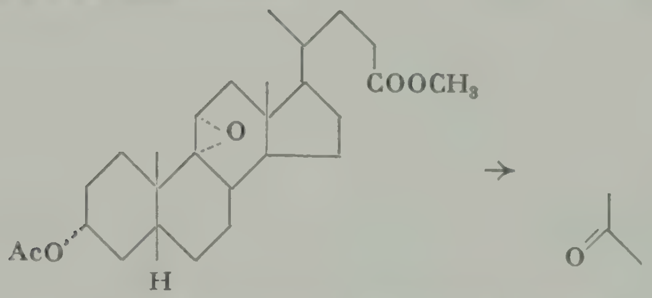
360. 

2-Thiazolylphenylcarbinol in glacial acetic acid treated with Na-dichromate in water, then refluxed 1 hr. → 2-benzoylthiazole. Y: 95%.

F. e. s. R. P. Kurkjy and E. V. Brown, Am. Soc. *74*, 6260 (1952); method s. M. Erne and H. Erlenmeyer, Helv. *31*, 652 (1948); **partial oxidation of steroids** s. S. H. Eppstein et al., Am. Soc. *76*, 3174 (1954).

Ketones from acoxy compounds CHOAc → CO

1.

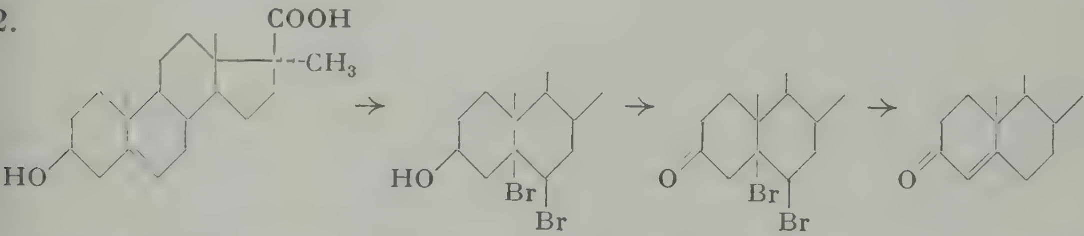


A soln. of Na-dichromate dihydrate in glacial acetic acid added to a soln. of methyl 3α-acetoxy-9α,11α-oxidocholanate in the same solvent, and allowed to stand 12 hrs. at room temp. → methyl 3-keto-9α,11α-oxidocholanate (startg. m. f. 596). Y: 89%. H. Heymann and L. F. Fieser, Am. Soc. *73*, 5252 (1951).

Chromic acid CrO_3

Ketones from sec. alcohols CHOH → CO

2.



with protection of carbon carbon double bonds. A soln. of Br in glacial acetic acid added dropwise to a soln. of 3.8 g. 17α-methyl-3β-hydroxy-Δ^5-etienic acid in glacial acetic acid containing Na-acetate, then a soln. of CrO_3 in 90%-acetic acid added, after 12 hrs. excess CrO_3 decomposed by cautious addition of methanol, then warmed with Zn-dust at 90° for 20 min. with vigorous agitating → 2.52 g. 17α-methyl-3-keto-Δ^4-etienic acid. H. H. Günthard et al., Helv. *35*, 2437 (1952).

large batches s. H. H. Inhoffen, H. Jahnke, and P. Nehring, B. *87*, 1154 (1954)

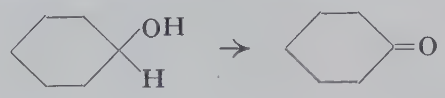
with Beckmann mixture s. *1*, 167; s. a. R. Grewe, W. Lorenzen, and L. Vining, B. *87*, 793 (1954)

Chromic acid-pyridine complex CrO_3-C_5H_5N

s. *8*, 325; s. a. W. F. Johns, R. M. Lukes, and L. H. Sarett, Am. Soc. *76*, 5026 (1954); W. S. Allen, S. Bernstein, and R. Littell, Am. Soc. *76*, 6116 (1954)

tert-Butyl hypochlorite *$(CH_3)_3C{\cdot}OCl$*

Oxidation of alcohols ←
Oxo compounds and carboxylic acid esters from alcohols
Aldehydes from α-hydroxycarboxylic acids

363. 

$$2\ n\text{-}C_5H_{11}CH_2OH \rightarrow n\text{-}C_5H_{11}CH_2OCOC_5H_{11}\text{-}n$$

tert-Butyl hypochlorite is superior to N-chlorosuccinimide. The oxidations proceed smoothly in pyridine. Sec. alcohols are dehydrogenated to ketones, mandelic acid being simultaneously decarboxylated to form benzaldehyde (Y: 99%), which is also obtained from benzyl alcohol. Other prim. alcohols are oxidized to esters of the corresponding acid.—E: Cyclohexanol and pyridine in CCl_4 treated dropwise with *tert*-butyl hypochlorite, cooled to -5^0 when the temp. starts to rise → cyclohexanone. Y: 90.5%.—Similarly at 31°: n-Hexanol → n-hexyl caproate. Y: 83%. F. e. s. C. A. Grob and H. Schmid, Helv. *36*, 1763 (1953).

Ketones from sec. alcohols CHOH → CO
s. *9*, 617

Oxidation-chlorination CH(OH)CH → COCCl
α-Chloroketones from alcohols
s. *9*, 618

Manganese dioxide *MnO_2*

Unsatd. oxo compounds from unsatd. alcohols CHOH → CO
s. *8*, 326, 465; steroids in chloroform s. F. Sondheimer, C. Amendolla, and G. Rosenkranz, Am. Soc. *75*, 5930, 5932 (1953); Soc. *1954*, 1226; in benzene s. D. Taub et al., Am. Soc. *76*, 4094 (1954); aliphatic compounds in acetone s. H. H. Inhoffen et al., A. *580*, 7 (1953); f. e. and limitations s. D. L. Turner, Am. Soc. *76*, 5175 (1954)

Potassium permanganate *$KMnO_4$*

Ketocarboxylic acids from hydroxyaldehydes ←

364. $C_6H_5CH(OH)CH_2CH_2CH_2CHO \rightarrow C_6H_5COCH_2CH_2CH_2COOH$

A satd. soln. of $KMnO_4$ added portionwise with shaking at room temp. to an aq. suspension of δ-phenyl-δ-hydroxyvaleraldehyde containing 2 drops of 10%-NaOH until the permanganate color persists for 30 min. → γ-benzoylbutyric acid. Y: 90%. C. W. Smith, D. G. Norton, and S. A. Ballard, Am. Soc. *73*, 5273 (1951).

Oxygen ↑ OC⇑O

Potassium hydroxide/alcohol *KOH*

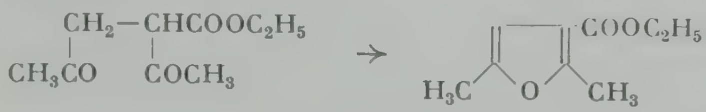
Oxido compounds from glycol monoesters via glycol acetate methanesulfonates

s. *9*, 206

Sodium/alcohol *NaOR*

Furan ring from γ-diketones

5.



Ethyl α-acetyllevulinate added to a cold soln. of Na in abs. ethanol, and worked up after 18 hrs. at room temp. → ethyl 2,5-dimethylfuran-3-carboxylate. Y: 83%. R. M. Acheson and R. Robinson, Soc. *1952*, 1127.

Alkali acetate ←

Oxazolones ←
Erlenmeyer reaction

with K-acetate s. *3*, 325; with Na-acetate s. J. P. Lambooy, Am. Soc. *76*, 133 (1954)

Sodium acetate/acetic anhydride *$CH_3COONa/(CH_3CO)_2O$*

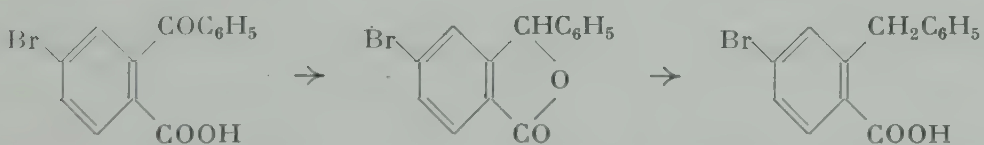
Enollactones from ketocarboxylic acids

s. *8*, 329; s. a. L. B. Barkley et al., Am. Soc. *76*, 5014 (1954).

Zinc amalgam *Zn,Hg*

Carboxylic acids from ketocarboxylic acids via phthalides CO → CH_2

36.

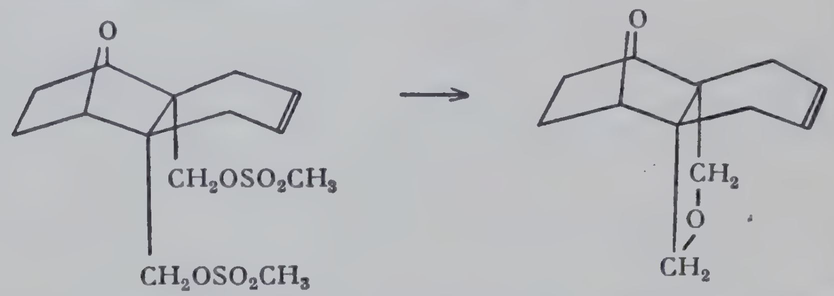


2-Benzoyl-4-bromobenzoic acid refluxed 24 hrs. with Zn-amalgam in aq. HCl and toluene → 5-bromo-α-phenylphthalide (Y: 95%) heated 7 hrs. with red P and iodine in *propionic acid* containing a little water → 2-benzyl-4-bromobenzoic acid (Y: 84%). F. e. s. E. D. Bergmann and E. Loewenthal, Bl. *1952*, 66; one-step procedure for halogen-free compounds s. Synth. Meth. *9*, 105.

Lithium aluminum hydride *$LiAlH_4$*

O-Heterocyclics from disulfonic acid esters ○

367.

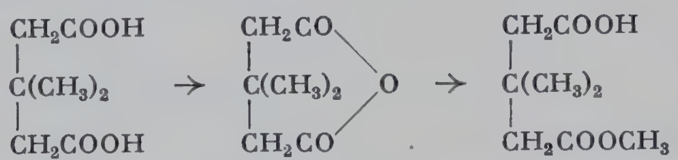


A soln. of dimesylate in tetrahydrofuran stirred into a soln. of $LiAlH_4$ in the same solvent, and refluxed 4 hrs. → cyclic oxide. Y: 83%. G. Stork et al., Am. Soc. *75*, 384 (1953).

Acetic anhydride *$(CH_3CO)_2O$*

Dicarboxylic acid monoesters from dicarboxylic acids via dicarboxylic acid anhydrides

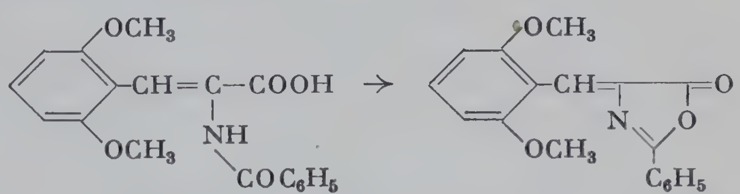
368.



β,β-Dimethylglutaric acid refluxed 1 hr. with acetic anhydride → *β,β*-dimethylglutaric anhydride (Y: ca. 100%) finely ground, added slowly at 0° to a well-stirred soln. of Na in methanol, allowed to warm slowly to room temp., and after a further hr. gently refluxed for 1 hr. → methyl hydrogen *β,β*-dimethylglutarate (Y: ca. 100%). S. F. Birch et al., Soc. *1952*, 1363; s. a. V. du Vigneaud and G. L. Miller, Biochem. Prep. *2*, 79 (1952).

Oxazolones from acylaminocarboxylic acids

369.



2-Benzamido-3-(2,6-dimethoxyphenyl)acrylic acid (m. 246-7°) heated with acetic anhydride 15 min. on a steam bath → 4-(2,6-dimethoxybenzylidene)-2-phenyl-5-oxazolone. Y: ca. 100%. Also isomer s. J. P. Lambooy, Am. Soc. *76*, 133 (1954).

Formic acid/hydrochloric acid *HCOOH/HCl*

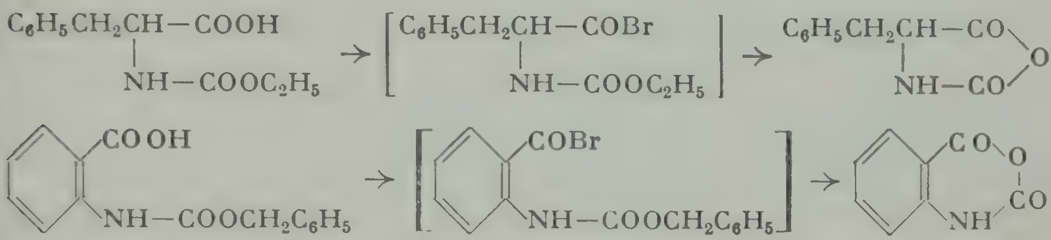
s. Hydrochloric acid/formic acid

Oxalic acid *$(COOH)_2$*

Furans from γ-diketones
s. *9*, 892

Phosphorus tribromide *PBr_3*

N-Carboxyaminocarboxylic acid anhydrides from N-carbalkoxyaminocarboxylic acids



PBr_3 added slowly to N-carbethoxy-DL-phenylalanine in anhydrous ether, and kept 12 hrs. at room temp. → N-carboxy-DL-phenylalanine anhydride. Y: 82%.—Similarly from N-carbobenzoxyanthranilic acid after 24 hrs. → isatoic anhydride. Y: ca. 90%.—The acid bromides cyclize more readily than the acid chlorides. F. e. s. D. Ben-Ishai and E. Katchalski, Am. Soc. *74*, 3688 (1952).

Phosphorus oxychloride *$POCl_3$*

Dicarboxylic acid anhydrides from dicarboxylic acids
s. *9*, 650

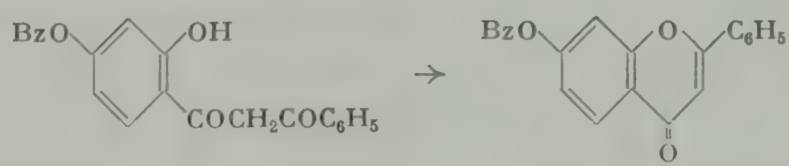
Potassium hydrogen sulfate *$KHSO_4$*

Ring closure to O-heterocyclics

s. *6*, 301; s. a. A. J. Weinheimer, S. W. Kantor, and C. R. Hauser, J. Org. Chem. *18*, 801 (1953)

p-Toluenesulfonic acid *TsOH*

Chromone ring from o-hydroxy-β-diketones

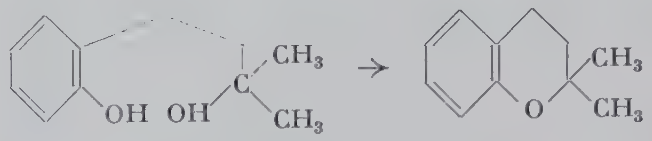
1. 

4-Benzoyloxy-2-hydroxydibenzoylmethane in xylene containing a trace of p-toluenesulfonic acid refluxed 10 hrs. in a Soxhlet apparatus con-

taining anhydrous Mg-sulfate in the thimble → 7-benzoyloxyflavone. Y: 79%. F. e. s. W. Baker, W. D. Ollis, and V. D. Poole, Soc. *1952*, 1505.

Sulfuric acid *H_2SO_4*

Chromans

372. 

A soln. of 2-methyl-4-(2-hydroxyphenyl)-2-butanol in acetic acid treated with 20%-H_2SO_4, and refluxed 0.5 hr. → 2,2-dimethylchroman. Y: 85%. M. Hallet and R. Huls, Bl. Soc. chim. Belg. *61*, 33 (1952).

Hydrochloric acid *HCl*

Cyclic ethers from diols

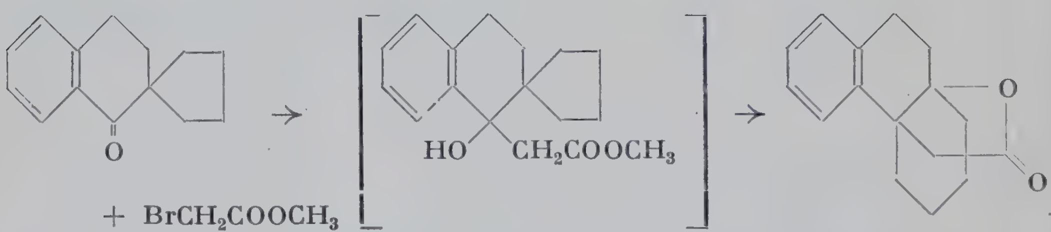
s. *6*, 302; s. a. H. C. Brown and K. LeRoi Nelson, Am. Soc. *75*, 24 (1953)

Chromone ring from o-hydroxy-β-diketones

s. *1*, 546; s. a. H. Schmid and H. Seiler, Helv. *35*, 1990 (1952)

Hydrochloric acid/formic acid *HCl/HCOOH*

Reformatskii synthesis
with subsequent
Wagner-Meerwein rearrangement
Synthesis of lactones from ketones

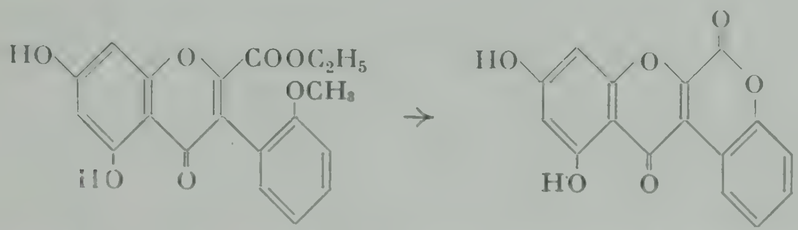
373. 

2,2-Tetramethylene-1-tetralone allowed to react with granulated Zn and methyl bromoacetate in benzene-ether, containing a crystal of iodine, at reflux temp. for 3.5 hrs., the crude product dissolved in anhydrous formic acid containing 2 drops of concd. HCl, and heated 45 min. on a steam bath → 4a-carboxymethyl-10a-hydroxy-1,2,3,4,4a,-9,10,10a-octahydrophenanthrene lactone. Y: 58% based on unrecovered ketone. B. Belleau, Am. Soc. *75*, 1159 (1953).

Hydrobromic acid *HBr*

Coumarin ring
Lactones from alkoxycarboxylic acid esters
Chromono(2′,3′:3,4)coumarins

4.



2-Carbethoxy-5,7-dihydroxy-2′-methoxyisoflavone, acetic acid, and HBr (d. 1.5) heated 2 hrs. at 140° → crude 5′,7′-dihydroxychromono-(2′3′:3,4)coumarin. Y: 90%. W. Baker, J. B. Harborne, and W. D. Ollis, Soc. *1953*, 1860.

Nitrogen ↑ **OC ⇑ N**

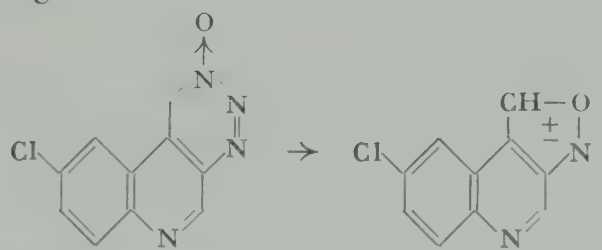
Sodium acetate *CH_3COONa*

Benzothioxol-2-ones ○
s. *9*, 55

Hydrochloric acid *HCl*

Isoxazole ring from
1,2,3-triazine ring

5.

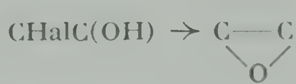


0.5 g. 6-chloro-1,2,3,9-tetraazaphenanthrene 3-oxide and concd. HCl left together for 12 hrs., then basified with NH_3 → 0.43 g. 6′-chloroquinolino(3′,4′:3,4)isoxazole (startg. m. f. 205). D. W. Ockenden and K. Schofield, Soc. *1953*, 1915.

Halogen ↑ **OC ⇑ Hal**

Sodium hydroxide *NaOH*

Oxido compounds from halogenhydrins

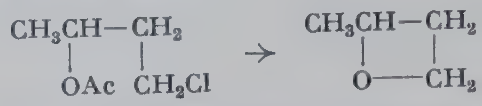


s. *9*, 916

Oxidoketones from halogenolactols ←
s. *9*, 596

Potassium hydroxide *KOH*

Cyclic ethers from acoxyhalides ○

376. 

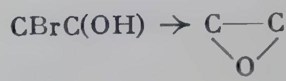
4-Chloro-2-butyl acetate added dropwise with vigorous stirring during 3 hrs. at an oil bath temp. of 120-140° to aq. 90%-KOH with distillation of the product formed, heating continued 30 min. at an oil bath temp. of 160° → 1,3-butylene oxide. Y: 66%. F. Sondheimer and R. B. Woodward, Am. Soc. 75, 5438 (1953).

Potassium carbonate *K_2CO_3*

Lactones from halogenocarboxylic acids ○

s. 4, 281; oxalactones s. M. G. J. Beets and W. Meerburg, R. 72, 411 (1953)

Silver oxide/pyridine *Ag_2O/C_5H_5N*

Oxido compounds from bromohydrins 

s. 9, 60

Silver acetate *CH_3COOAg*

Oxidoketones from halogenolactolides ←

s. 9, 596

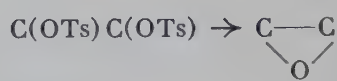
Sulfur ▲ OC ⇑ S

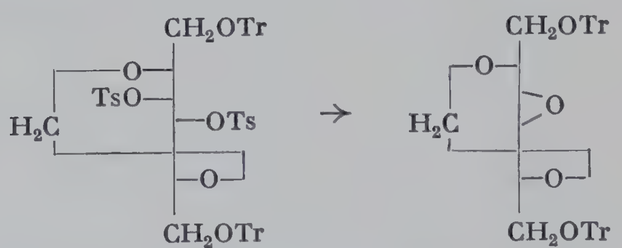
Without additional reagents *w.a.r.*

Oxazoline-2-thiols from bishydroxythiuram disulfides ○

s. 9, 412

Potassium hydroxide *KOH*

3,4-Anhydroglycitols 

377. 

2,5-Methylene-3,4-ditosyl-1,6-ditrityl-D-mannitol refluxed with KOH in ethanol-water on a steam bath for 2 days → 3,4-anhydro-2,5-methylene-1,6-ditrityl-D-talitol. Y: 83%. S. B. Baker and G. Kohanyi, Am. Soc. 75, 2140 (1953).

Nickel *Ni*

γ-Lactones from
γ,γ-disulfonylcarboxylic acids ○

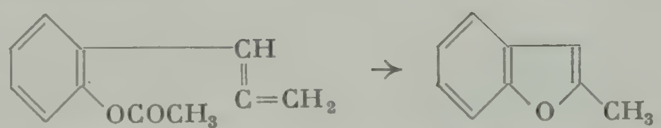
8.


4.4-Bis(ethylsulfonyl)-7-methyloctanoic acid in 4%-NaOH shaken and heated at 220° with Raney-Ni for 8 hrs. at 2500 p.s.i. H_2 → 4-hydroxy-7-methyloctanoic acid lactone. Y: 87%. Formation of carboxylic acids in other cases s. M. W. Cronyn, Am. Soc. *74*, 1225 (1952); cf. *9*, 880.

Carbon ↑ OC ⇑ C

Sodium/alcohol *NaOR*

Furan ring from allenes ○

9.


o-Allenylphenol acetate added to a soln. of Na in abs. methanol, and refluxed 11 hrs. → 2-methylbenzofuran. Y: 81%. R. Gaertner, Am. Soc. *73*, 4400 (1951).

Oxalic acid *(COOH)₂*

Ketones from enolethers C:C(OR) → CHCO
s. *9*, 86

N-Bromosuccinimide $\left.\begin{matrix} CH_2-CO \\ CH_2-CO \end{matrix}\right\rangle NBr$

Oxo compounds from
α-hydroxycarboxylic acids C(OH)COOH → CO

0.
$$(C_6H_5)_2C\begin{matrix} OH \\ COOH \end{matrix} \rightarrow (C_6H_5)_2CO$$

Benzilic acid and N-bromosuccinimide refluxed 30 min. in water → benzophenone. Y: 85-90%. F. e. s. M. Z. Barakat and M. F. Abd El-Wahab, Am. Soc. *75*, 5731 (1953).

Ozone/periodate O_3/IO_4^-

Degradation of α,β-ethylene-γ-lactones ←
to carboxylic acids via α-hydroxyketones
s. *4*, 282; s. a. Pharm. Acta Helv. *27*, 287 (1952)

Sulfuric acid H_2SO_4

Ketones from enolethers C:C(OR) → CHCO

s. *9*, 87; s. a. A. J. Speziale, J. A. Stephens, and Q. E. Thompson, Am. Soc. *76*, 5011 (1954).

tert-Butyl hypochlorite $(CH_3)_3C{\cdot}OCl$

Aldehydes from α-hydroxycarboxylic acids CH(OH)COOH → CHO

s. *9*, 363

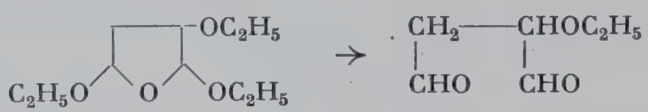
Periodate/ozone s. Ozone/periodate IO_4^-/O_3

Hydrochloric acid *HCl*

Lactones from halogenocarboxylic acid esters with simultaneous replacement of carbalkoxy groups by hydrogen ←

s. *9*, 607

Alkoxydialdehydes from 2,3,5-trialkoxytetrahydrofurans C

381. 

2,3,5-Triethoxytetrahydrofuran (prepn. s. 234) dissolved in 0.1 *N* aq. HCl, and warmed 20 min. at 70-75° → O-ethylmalic dialdehyde (Y: 85.7% as the 4-nitrophenylhydrazone). F. e. s. A. Stoll, A. Lindenmann, and E. Jucker, Helv. *36*, 1500 (1953).

Formation of N—N Bond

Exchange

Hydrogen ↑ NN⇅H

Sodium nitrite $NaNO_2$

Diazonium fluoborates $\cdot N_2^+ BF_4^-$

s. *9*, 129

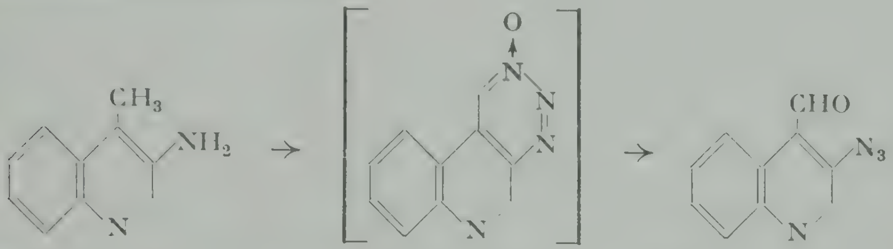
N-Nitrosation NH → N·NO

s. *7*, 413; *8*, 369; s. a. C. M. Samour and J. P. Mason, Am. Soc. *76*, 441 (1954)

Azides from amines $NH_2 \rightarrow N_3$

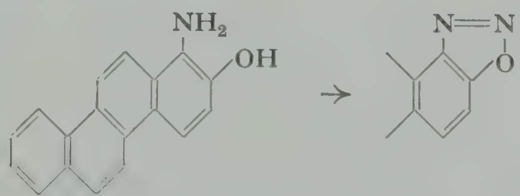
s. *8*, 363; s. a. Am. Soc. *75*, 6335 (1953)

o-Azidoaldehydes from o-aminomethyl derivatives ←



1 g. 3-aminolepidine treated with aq. $NaNO_2$ in HCl, kept overnight at 0°, filtered, and basified → 0.75 g. 3-azidoquinoline-4-aldehyde (startg. m. f. 170). Also isolation of the intermediate (cf. 425) s. D. W. Ockenden and K. Schofield, Soc. *1953*, 1915.

Diazo oxides from aminophenols ←



32%-HCl added at 0-5° to a soln. of 400 mg. 1-amino-2-hydroxychrysene in *dimethylformamide*, then aq. $NaNO_2$ added slowly with vigorous stirring, and allowed to stand 0.5 hr. → 370 mg. 1,2-chrysenequinone-1-diazide. F. e. and methods s. O. Süs et al., A. *579*, 133 (1953).

Influence of substituents on the Widman-Stoermer cinnoline synthesis ○

s. *1*, 322; s. a. A. J. Nunn and K. Schofield, Soc. *1953*, 3700

Sodium nitrite/nitric acid *$NaNO_2/HNO_3$*

N-Nitrosourethans from urethans $NH \rightarrow N{\cdot}NO$

$$CH_3CH{=}CHCH_2NHCOOC_2H_5 \rightarrow CH_3CH{=}CHCH_2N(NO)COOC_2H_5$$

Aq. $NaNO_2$ and ice added to a mixture of N-crotylurethan and ether, then cold 35%-HNO_3 added during 1-1.5 hrs. through a funnel with an extension tube reaching to the bottom of the flask, with occasional swirling and addition of ice to keep the temp. below 15°, allowed to stand 12 hrs., the ether layer separated, washed with water, then with $NaHCO_3$ → N-nitroso-N-crotylurethan. Y: 75%. F. e. s. D. Y. Curtin and S. M. Gerber, Am. Soc. *74*, 4052 (1952); s. a. W. W. Hartman and R. Phillips, Org. Synth. Coll. Vol. *2*, 464 (1943).

Potassium nitrite KNO_2

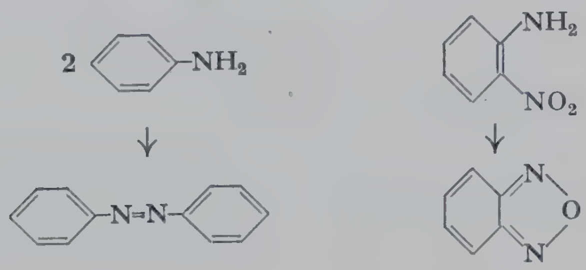
Tetrazoles from aminoguanidines

s. *8*, 362; thermal isomerization of 5-aminotetrazoles s. Am. Soc. *76*, 88 (1954)

Phenyl iodosoacetate $C_6H_5I(OAc)_2$

Oxidations with phenyl iodosoacetate ←
Azo compounds from amines
Benzofurazan oxides from o-nitramines

385.



Aniline	o-Nitraniline
added to a soln. of phenyl iodosoacetate in benzene and allowed to stand 2 days at room temp. →	
azobenzene. Y: 95%.	benzofuran oxide. Y: 81%.

F. e. s. K. H. Pausacker, Soc. *1953*, 1989; *1954*, 3122.

Stannous chloride $SnCl_2$

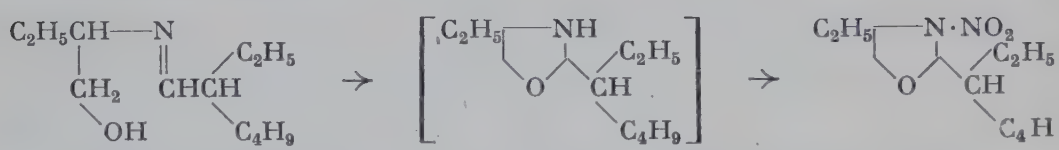
Hydrazines from amines $NH_2 \rightarrow NHNH_2$

s. *9*, 569

Nitrosyl chloride $NOCl$

Hydroxyazomethine-oxazolidine isomerization ←
3-Nitrosoöxazolidines

386.



NOCl allowed to distill into a mixture of 2-(2-ethylhexylideneamino)-1-butanol, dry pyridine, and ether cooled below 0°, then stirred 20 min. → 2-(3-heptanyl)-3-nitroso-4-ethyloxazolidine. Y: 76%.—2-Amino-alcohol-aldehyde anhydro products, regardless of structure, react with H-replacing reagents in anhydrous media to give derivatives of the oxazolidine form. F. e. and reactions s. E. P. Goldberg and H. R. Nace, Am. Soc. *75*, 6260 (1953).

Sulfuric acid *H_2SO_4*

N-Nitration $NH \rightarrow N \cdot NO_2$

N-Nitramines s. 8, 365; N-nitroisothioureas s. L. Fishbein and J. A. Gallaghan, Am. Soc. *76*, 1877 (1954)

Oxygen ↑ NN⇅O

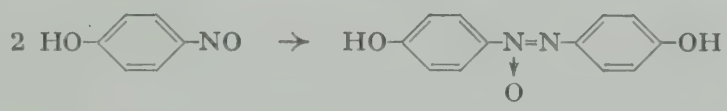
Acetic acid *CH_3COOH*

Azo compounds from nitroso compounds and amines $RNO + H_2NR' \rightarrow RN{:}NR'$

s. *1*, 265; *2*, 303; *3*, 252; s. a. C. M. Atkinson et al., Soc. *1954*, 2023

Benzenesulfonyl chloride/pyridine *$C_6H_5SO_2Cl/C_5H_5N$*

Azoxy compounds from nitroso compounds $2\,ArNO \rightarrow ArN(O){:}NAr$



A mixture of p-quinonemonoxime with benzenesulfonyl chloride in pyridine allowed to stand 12 hrs. at 25°, then heated 20 min. on a steam bath, cooled, and acidified with 25%-H_2SO_4 → p-azoxyphenol. Y: 45%. N. J. Leonard and J. W. Curry, J. Org. Chem. *17*, 1071 (1952).

Elimination

Hydrogen ↑ NN⇑H

Silver oxide *Ag_2O*

Diazo compounds from hydrazones $C{:}N \cdot NH_2 \rightarrow C{:}N_2$

cf. *3*, 255; with Ag_2O in place of HgO s. W. Schroeder and L. Katz, J. Org. Chem. *19*, 718 (1954)

Alkyl nitrite *RONO*

Tetrazolium salts from formazans ○

s. *6*, 329; f. methods s. J. N. Ashley et al., Soc. *1953*, 3881; cf. H. Seiler and H. Schmid, Helv. *37*, 1 (1954)

Carbon ↑ **NN ⇑ C**

Lead tetraacetate *$(CH_3COO)_4Pb$*

○

Tetrazoles from
3,6,9-tricarbaundecaz-1,3,8,10-tetraenes

388.

A soln. of Pb-tetraacetate in chloroform added to a soln. of 6-imino-1,3,9,11-tetraphenyl-3,6,9-tricarbaundecaz-1,3,8,10-tetraene in the same solvent, and warmed gently for a few min. → 2,5-diphenyltetrazole. Y: ca. 100%. F. L. Scott, D. A. O'Sullivan, and J. Reilly, Am. Soc. *75*, 5309 (1953).

Formation of N—Hal Bond

Exchange

Hydrogen ↑ **NHal ⇅ H**

Silver trifluoroacetate *CF_3COOAg*

N-Halogenation CONH → CONHa

Perfluoro-N-halogenodicarboxylic acid imides s. *7*, 372; halogenated N-bromoacetamides s. J. D. Park et al., Am. Soc. *74*, 2189 (1952)

Silver salt *Ag^+*

N-Iododicarboxylic acid imides >NI

389.

49.5 g. powdered Ag salt of succinimide added portionwise with stirring at 5-10° to a soln. of iodine in acetone, and the product isolated after 30 min. when the color has disappeared → 43 g. N-iodosuccinimide (startg. m. f. 641). C. Djerassi and C. T. Lenk, Am. Soc. *75*, 3493 (1953)

Formation of N—S Bond

Uptake

Addition to Oxygen and Nitrogen NS ⇓ ON

Without additional reagents *w.a.r.*

Sulfamic acids from hydroxylamines $NHOH \rightarrow NHSO_3H$

0. $$(CH_3)_2CHNHOH + SO_2 \rightarrow (CH_3)_2CHNHSO_3H$$

SO_2 passed rapidly into a soln. of N-isopropylhydroxylamine in chloroform for a few min. → isopropylsulfamic acid. Y: 60%. F. e. s. A. I. Ryer and G. B. L. Smith, Am. Soc. *73*, 5675 (1951).

Addition to Sulfur NS ⇓ S

Hydrazoic acid *HN_3*

Sulfoximines from sulfoxides $>S\rightarrow O \rightarrow >S\genfrac{}{}{0pt}{}{\nearrow O}{\searrow NH}$

s. *8*, 370; s. a. D. Jerchel, L. Dippelhofer, and D. Renner, B. *87*, 947 (1954)

Exchange

Oxygen ↑ NS ⇅ O

Without additional reagents *w.a.r.*

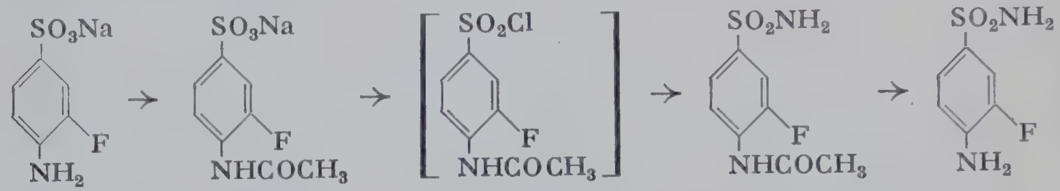
Sulfonic acid amides from sulfonic acid anhydrides $SO_2N<$

1. $$CH_3SO_2\cdot O\cdot SO_2CH_3 + 2\,C_6H_5NH_2 \rightarrow CH_3SO_2NHC_6H_5 + CH_3SO_3^-\ C_6H_5\overset{+}{N}H_3$$

Aniline added to a soln. of methanesulfonic anhydride (prepn. s. 177) in benzene whereupon anilinium methanesulfonate separates immediately (Y: 97%), and worked up after 15 min. → methanesulfonic acid anilide. Y: 96%. F. e. s. H. G. Khorana, Can. J. Chem. *31*, 585 (1953).

Via intermediates *v.i.*

Aminosulfonic acid amides ←
from aminosulfonic acids
Protection of amino groups
Selective hydrolysis

392.


Acetic anhydride poured over dried Na-3-fluoro-4-aminobenzenesulfonate, then heated 1 hr. on a steam bath → Na-3-fluoro-4-acetaminobenzenesulfonate (Y:93%) mixed with PCl_5, the crude product isolated after 10 min., treated with aq. NH_3, and warmed on a water bath → 3-fluoro-4-acetaminobenzenesulfamide (Y: 81%) refluxed 30 min. with 20%-HCl → 3-fluoro-4-aminobenzenesulfamide (Y: 92%). F. e. s. K. Kraft and F. Dengel, B. *85*, 577 (1952).

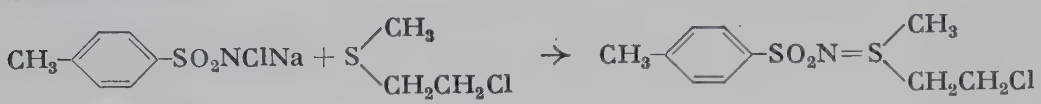
Halogen ↑ NS⇅Hal

Without additional reagents *w.a.r.*

Sulfonic acid amides $SO_2Cl \rightarrow SO_2N<$
from sulfonic acid chlorides

s. *9*, 392

Sulfidimides ←

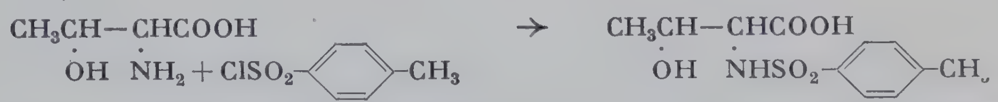
393.


2-Chloroethyl methyl sulfide shaken with an aq. soln. of chloramine-T until precipitation is complete → p-toluenesulfonyl-2-chloroethylmethylsulfidimide. Y: 82%. F. e. s. J. K. Whitehead and H. R. Bentley, Soc. *1952*, 1572.

Sodium hydroxide *NaOH*

Sulfonic acid amides from $SO_2Cl \rightarrow SO_2N<$
sulfonic acid chlorides

s. *1*, 271; *4*, 299; N-tosylation s. H. Stetter and E.-E. Roos, B. *87*, 566 (1954); P. G. Katsoyannis and V. du Vigneaud, Am. Soc. *76*, 3113 (1954)

394.


Selective N-tosylation. Aq. NaOH and p-toluenesulfonyl chloride in ether added dropwise at 65-68° with vigorous stirring during 1 hr. to a soln.

of DL-threonine in aq. NaOH with removal of the ether by a slow stream of air, and stirring continued for 10 min. → N-tosyl-DL-threonine. Y: 78-82%.—A good yield is obtained only under carefully controlled conditions. M. Brenner, K. Rüfenacht, and E. Sailer, Helv. *34*, 2102 (1951).

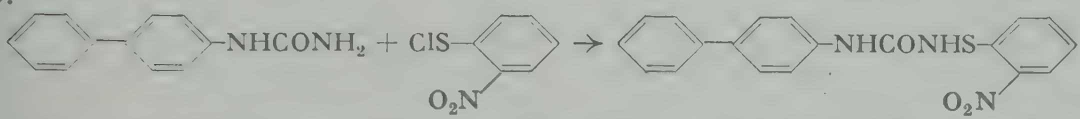
Disulmides $(RSO_2)_2NH$

s. *1*, 273; s. a. O. Süs et al., A. *579*, 133 (1953)

Pyridine *C_5H_5N*

Sulfenylureas from sulfenylchlorides SCl → SNHCONHR

5.



p-Diphenylylurea allowed to react with o-nitrobenzenesulfenyl chloride (added in 2 portions at 5 min. interval) at 50-40° for 20 min. → N-p-diphenylyl-N′-o-nitrobenzenesulfenylurea. Y: 75%. F. e. and methods s. F. Kurzer, Soc. *1953*, 3360.

Carbon ↑ NS⇅C

Without additional reagents *w.a.r.*

Cleavage of sulfonylnitro compounds ←

s. *9*, 141

Sulfamic acids from isocyanates, urethans, and ureas ←

96.

$C_2H_5N{=}C{=}O$ ↘ $+ H_2SO_4$ ↙ $C_2H_5NHCOOC_2H_5$

$C_2H_5NHSO_3H$

Ethyl isocyanate added dropwise with stirring and ice-cooling to 20%-oleum, the ice bath removed when ca. half of the isocyanate has been added, after the addition the lukewarm mixture chilled and poured slowly with ice-cooling and shaking into anhydrous ether whereby the product precipitates ↓

Ethyl ethylcarbamate added with stirring and ice-cooling to 60%-oleum, and slowly warmed on a water bath until at 60° CO_2-evolution occurs ↙

Y: 83% (Am. Soc. 75, 1405) ethylsulfamic acid Y: 93% (Am. Soc. 75, 1409)

F. e., also from ureas, s. T. I. Bieber, Am. Soc. *75*, 1405, 1409 (1953).

Formation of N—Rem Bond

Exchange

Hydrogen ↑ NRem ⇅ H

N-Chloramides ←

Phosphoric from phosphorous acid derivatives ←

397.

$$(C_2H_5O)_2P \cdot OH \rightarrow (C_2H_5O)_2P\begin{matrix} \diagup\!\!\diagup O \\ \diagdown NHC_6H_5 \end{matrix}$$

N-Chlorosuccinimide added to a soln. of diethyl phosphite in benzene, after 2 hrs. the precipitated succinimide removed by filtration, aniline added to the filtrate, and the product isolated after ca. 2 hrs. → diethyl anilinophosphonate. Y: 87%. Also pyrophosphates and hydrogen phosphates s. G. W. Kenner et al., Soc. *1952*, 3675, 3669.

Halogen ↑ NRem ⇅ Hal

Silver cyanide *AgCN*

Isocyanosilanes $\rangle$SiNC

398.

$$(CH_3)_3SiI + AgCN \rightarrow (CH_3)_3SiNC$$

Dry Ag-cyanide added with stirring during 1.5 hrs. to a mixture of trimethyliodosilane and benzene, stirring and refluxing continued for 2.5 hrs., cumene added as chaser, and distilled → trimethylisocyanosilane. Y: 80%. F. e. and reactions s. J. J. McBride, Jr., and H. C. Beachell, Am. Soc. *74*, 5247 (1952).

Carbon ↑ NRem ⇅ C

Without additional reagents *w.a.r.*

Cleavage of diarylmercury compounds ←

s. *7*, 383; s. a. Sint. Org. *2*, 136 (1952); C. A. *48*, 624 g

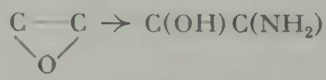
Formation of N—C Bond

Uptake

Addition to Oxygen and Carbon NC ⇓ OC

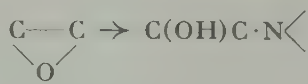
Without additional reagents *w.a.r.*

Aminoalcohols from oxido compounds
Aminosugars

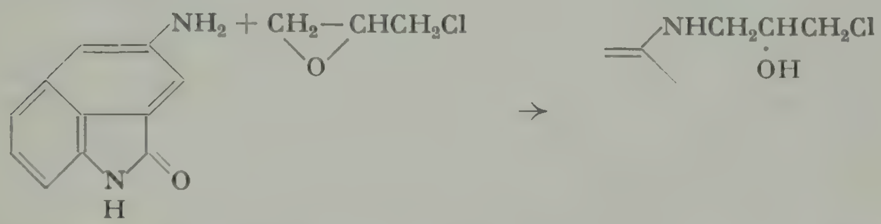


s. *2*, 319; s. a. B. R. Baker and R. E. Schaub, J. Org. Chem. *19*, 646 (1954)

Subst. halogenaminoalcohols from oxidohalides



399.



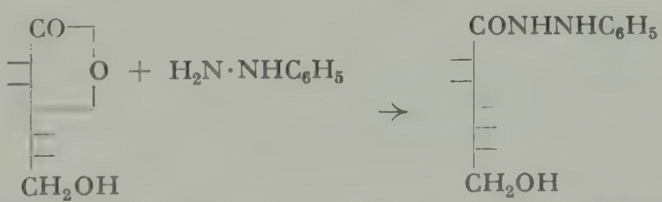
A suspension of 4-aminonaphthostyril in alcohol treated with epichlorohydrin, and refluxed overnight → sec. amine. Y: 80%. A. Stoll, T. Petrzilka, and J. Rutschmann, Helv. *35*, 1249 (1952).

Hydroxycarboxylic acid amides from lactones

s. *7*, 386; *8*, 384; s. a. J. Swidinsky, F. H. McMillan, and J. A. King. Am. Soc. *76*, 1148 (1954)
with pantolactone s. *3*, 24; s. a. M. Vernsten, W. C. Braaten, and M. B. Moore, Am. Soc. *76*, 5811 (1954)

Hydroxycarboxylic acid hydrazides from lactones
Carbohydrate derivatives

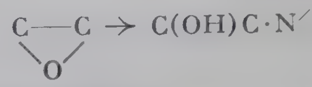
400.



D-Altro-D-*manno*-heptonic γ-lactone heated 2 hrs. on a steam bath with phenylhydrazine and water → D-altro-D-*manno*-heptonic phenylhydrazide. Y: almost 100%. D. A. Rosenfeld, N. K. Richtmyer, and C. S. Hudson, Am. Soc. *73*, 4907 (1951).

Pyridine *C_5H_5N*

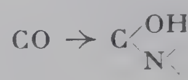
2-(Sulfonylamino)alcohols from oxido compounds



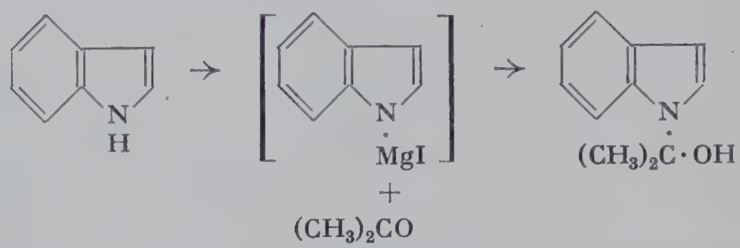
s. *6*, 348; s. a. D. I. Weisblat et al., Am. Soc. *75*, 5893 (1953)

Ethylmagnesium iodide *C_2H_5MgI*

1,1-Aminoalcohols from oxo compounds



401.



Acetone in ether added dropwise with stirring and ice-cooling to an ethereal soln. of indolyl-MgI (prepared from indole and ethyl-MgI), allowed to stand 20 min. at room temp., then heated 30 min. on a water bath → 1-(1-hydroxy-1-methylethyl)indole. Y: 75%. T. Hoshino, B. *85*, 858 (1952).

Addition to Nitrogen and Carbon NC ⇓ NC

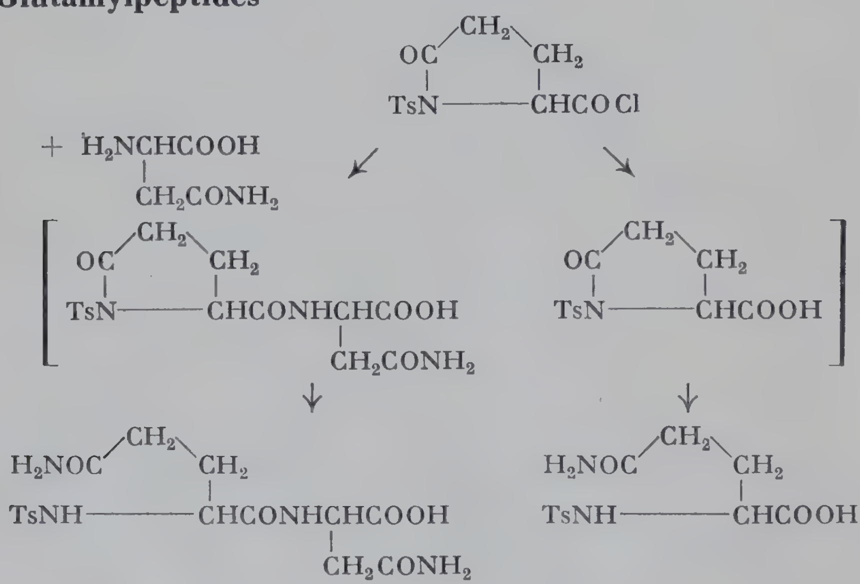
Without additional reagents *w.a.r.*

Acylureas from carbodiimides ←

s. *9*, 277

Subst. carboxylic acid amides and carboxylic acids from carboxylic acid chlorides with subsequent lactam ring opening
Glutamylpeptides

402.



1-Tosylpyroglutamyl chloride (prepn. s. 566)

added in portions with vigorous stirring during 15-20 min. at a pH above 8 to a mixture prepared by adding MgO at 50° to aq. L-asparagine and rapidly cooling in an ice-salt bath, allowed to stand 1.5 hrs. at room temp. with intermittent stirring, concd. HCl added, stirring resumed, crude tosyl-L-pyroglutamyl-L-asparagine isolated, dissolved in concd. aq. NH_3, allowed to stand 30-60 min., partially evaporated under reduced pressure to remove most of the NH_3, and acidified with concd. HCl → tosyl-L-glutaminyl-L-asparagine. Y: 83%.

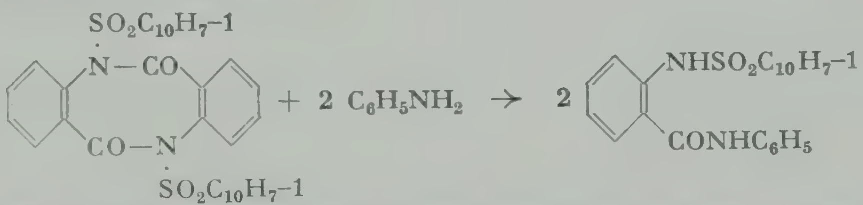
stirred vigorously for 1 hr. with a mixture of MgO, water, and ether, then concd. aq. NH_3 added, stirring continued for 30 min., partly evaporated under reduced pressure to remove most of the NH_3, and acidified → tosyl-L-glutamine (startg. m. f. 42). 24 g. from 33 g.

J. M. Swan and V. du Vigneaud, Am. Soc. *76*, 3110 (1954).

Hydantoin ring opening
s. *9*, 436

Dianthranilide ring opening

403.



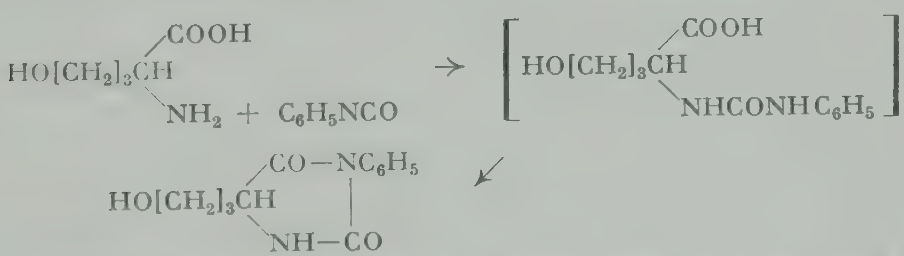
N,N′-Bis-(1-naphthalenesulfonyl)dianthranilide refluxed 3 hrs. with aniline → o-(1-naphthalenesulfonamido)benzanilide. Y: ca. 75%. A. Mustafa, Soc. *1952*, 2435.

Sodium hydroxide *NaOH*

Ureas from amines and isocyanates $NH_2 \rightarrow NHCONHR$
s. *3*, 267; s. a. K. Schlögl, F. Wessely, and G. Korger, M. *83*, 845 (1952)

Hydantoins from α-aminocarboxylic acids via α-ureidocarboxylic acids

404.



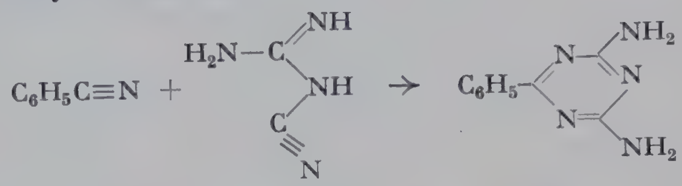
Phenylisocyanate added dropwise at room temp. to a soln. of DL-α-amino-δ-hydroxyvaleric acid in aq. NaOH, vigorously stirred for 15

min., and the resulting α-phenylureido-δ-hydroxyvaleric acid heated 1 hr. with HCl on a steam bath → 3-phenyl-5-γ-hydroxypropylhydantoin (startg. m. f. 570). Y: 89%. Also isolation of the intermediate s. R. Gaudry, Can. J. Chem. *29*, 544 (1951); in 2 steps s. a. K. Schlögl, F. Wessely, and G. Korger, M. *83*, 845 (1952).

Potassium hydroxide *KOH*

1,3,5-Triazines from nitriles and dicyanodiamide

405.

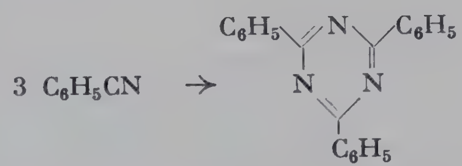


Dicyanodiamide and benzonitrile added to a soln. of 85%-KOH in Methyl Cellosolve heated with stirring, refluxing and stirring continued for 5 hrs. after the exothermic reaction, which starts at 90-110°. has subsided → 2,4-diamino-6-phenyl-s-triazine. Y: 75-95%. J. K. Simons and M. R. Saxton, Org. Synth. *33*, 13 (1953); with dialkoxyacetonitriles s. V. P. Wystrach and J. G. Erickson, Am. Soc. *75*, 6345 (1953).

Methyl alcohol *CH_3OH*

Trimerization of nitriles to 1,3,5-triazines

406.



A soln. of benzonitrile in an equal weight of methanol heated 18 hrs. at 125° under an initial pressure of 7500 atm. → 2,4,6-triphenyl-s-triazine. Y: 82%. F. e. s. T. L. Cairns, A. W. Larchar, and B. C. McKusick, Am. Soc. *74*, 5633 (1952).

Acetic acid *CH_3COOH*

Reactions with cyanogen
Sym. bisoxamidines from amines $\mathrm{RNHC(=HN)-)_2}$

407. $2\ n\text{-}C_4H_9NHCH_2CH_2NH_2 + (CN)_2 \downarrow$

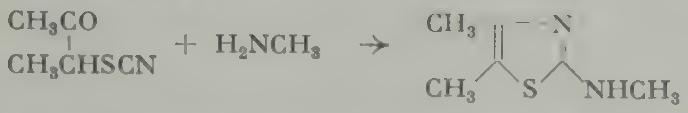
$$n\text{-}C_4H_9NHCH_2CH_2NH\underset{\underset{NH}{\|}}{C}-\underset{\underset{NH}{\|}}{C}NHCH_2CH_2NHC_4H_9\text{-}n$$

Cyanogen passed at room temp. into a soln. of N-n-butylethylenediamine in aq. acetic acid at pH 7-8 → sym-bis-(2-n-butylaminoethyl)-oxamidine. Y: 67%. F. e. and reactions, with lower yields, s. H. M. Woodburn and R. C. O'Gee, J. Org. Chem. *17*, 1235 (1952).

Hydrochlorides

2-Aminothiazoles from 2-ketothiocyanates

408.



A mixture of methylamine hydrochloride, water, and 3-thiocyano-2-butanone refluxed 8 hrs. → 2-methylamino-4,5-dimethylthiazole. Crude Y: 77%. F. e. s. R. A. Mathes and J. T. Gregory, Am. Soc. *74*, 3867 (1952).

Hydrochloric acid *HCl*

Acylsemicarbazides from carboxylic acid hydrazides ←

409.

$$\begin{array}{l} CONHNH_2 \\ | \\ CONHNH_2 \end{array} + 2\ KNCO \rightarrow \begin{array}{l} CONHNHCONH_2 \\ | \\ CONHNHCONH_2 \end{array}$$

A soln. of oxalic acid dihydrazide in HCl treated with aq. KNCO, and allowed to stand a short time → oxalic acid disemicarbazide. Y: 95%. H. Gehlen, A. *577*, 237 (1952).

2-Mercaptoimidazoles

s. *5*, 252; 4,5-imidazoledicarboxylates s. Am. Soc. *74*, 1085 (1952)

1,3,5-Triazines from nitriles by trimerization

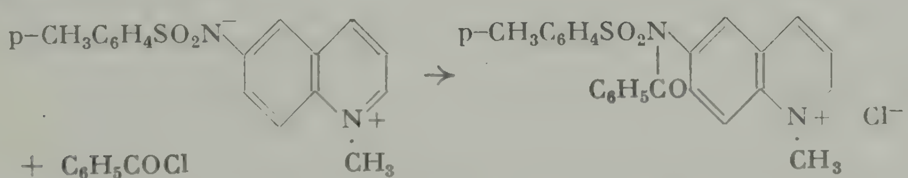
s. *3*, 277; mixed trimerization s. J. Hechenbleikner, Am. Soc. *76*, 3032 (1954)

Addition to Halogen and Carbon NC ⇓ HalC

Without additional reagents *w.a.r.*

Quaternary ammonium salts from betaineazeniates ←

410.



A mixture of 6-(p-tolylsulfonamido)quinoline methylbetaine and benzoyl chloride heated 1 hr. at 125-130° → 6-(N-benzoyl-p-tolylsulfonamido)quinoline methochloride. Y: 90%. Also with alkyl halides s. A. M. Simonov, Ж. *22*, 2006 (1952); C. A. *47*, 9328g.

Addition to Sulfur and Carbon

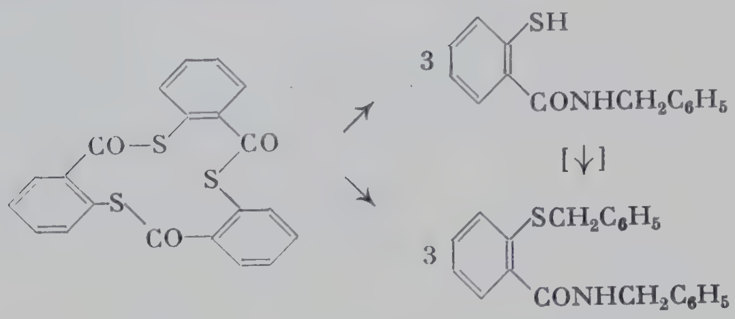
NC ⇓ SC

Without additional reagents *w.a.r.*

←

Thiosalicylide ring opening
Thioethers from amines

411.



Tri(thiosalicylide) and benzylamine

in benzene refluxed 7 hrs. under N_2 → N-benzylthiosalicylamide. Y: 79%.

and a trace of NH_4Cl boiled 3 hrs. → N,S-dibenzylthiosalicylamide. Y: 90%.

F. e. s. W. Baker, A. S. El-Nawawy, and W. D. Ollis, Soc. *1952*, 3163.

Triethylamine *$(C_2H_5)_3N$*

Dithiocarbamic acid esters from amines

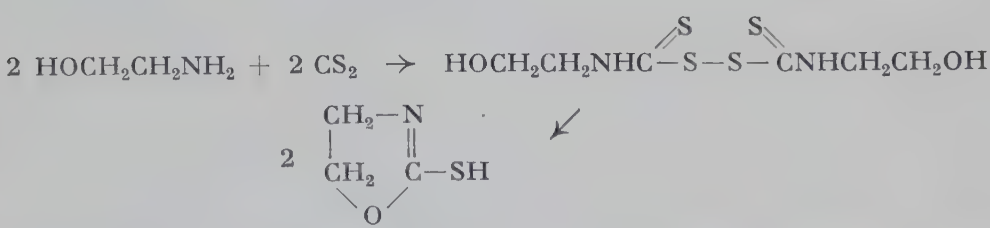
$\mathrm{NH_2} \rightarrow \mathrm{NHC}\langle^{S}_{SR}$

s. *9*, 705

Iodine *I*

Oxazoline-2-thiols from 2-aminoalcohols via bishydroxythiuram disulfides

412.



CS_2 added in small portions at 0° to a soln. of ethanolamine in methanol, then a methanolic soln. of iodine added to a faint permanent yellow color → bis-(2-hydroxyethyl)thiuram disulfide (Y: 92%) suspended in water and heated to boiling during 1 hr. → oxazoline-2-thiol (Crude Y: 42%).—The method generally employed to prepare these heterocyclics results in some instances in the formation of thiazoline-2-thiols. F. e. s. A. A. Rosen, Am. Soc. *74*, 2994 (1952).

Addition to Carbon NC ⇓ CC

Without additional reagents *w.a.r.*

Amines from ethylene derivatives C:C → CHCN<

s. *6*, 364; s. a. L. H. Sternbach and S. Kaiser, Am. Soc. *74*, 2215 (1952)

1,2-Nitrochlorides from ethylene derivatives C:C → CClC(NO_2)

s. *1*, 289; s. a. H. Shechter et al., Am. Soc. *74*, 3052 (1952)

Enamines from acetylene derivatives C:C → CH:CN<

s. 7. 217; β-amino-α,β-ethylenealdehydes s F. Wille and F. Knörr, B. *85*, 841 (1953)

1,2-Nitramines from α,β-nitroethylene derivatives and azomethines C(NO_2)C·N<

413. $C_6H_5C(NO_2){=}CHC_6H_5 + H_2NC_6H_5$ ↘ ; $C_6H_5CH_2NO_2 + C_6H_5CH{=}NC_6H_5$ ↙

$C_6H_5CH(NO_2){-}CH(NHC_6H_5)C_6H_5$

Aniline added to a suspension of α-nitrostilbene in abs. ethanol, and allowed to stand 2 days at room temp.

Phenylnitromethane and a little diethylamine added with ice-cooling to a soln. of benzylideneaniline in abs. ethanol, and allowed to stand 10 days in an ice box

1-nitro-2-anilino-1,2-diphenylethane

Y: 90.5% Y: 91%

F. e. s A. Dornow and F. Boberg, A. *578*, 94 (1952).

Aliphatic 1,2-dinitro compounds from ethylene derivatives C:C → C(NO_2)C(NO_2)

s. *3*, 279; s. a. R. N. Haszeldine, Soc. *1953*, 2075

1,2,3-Triazoles from acetylene derivatives ○

s. *8*, 404; with hydrazoic acid s. L. W. Hartzel and F. R. Benson, Am. Soc. *76*, 667 (1954)

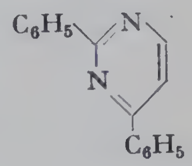
Sodium *Na*

Amines from ethylene derivatives $C{:}C \rightarrow CHCN\langle$

s. *6*, 367/8; also prim. and sec. amines, addition to ethylene, use of K and NaH s. B. W. Howk, Am. Soc. *76*, 1899 (1954)

Potassium *K*

Pyrimidines from nitriles and acetylene ○

414. $2\ C_6H_5CN + HC{\equiv}CH \rightarrow$ 

Benzonitrile and K treated with acetylene at a gage pressure of 10-15 atm. for 14 hrs. at 180-200° → 2,4-diphenylpyrimidine. Y: 51%. F. e., with lower yields, s. T. L. Cairns, J. C. Sauer, and W. K. Wilkinson, Am. Soc. *74*, 3989 (1952).

Sodium azide NaN_3

Azides from ethylene derivatives $C{:}C \rightarrow CHC(N_3)$

415. $$C_6H_5CH{=}CHNO_2 \rightarrow \underset{N_3}{C_6H_5CH}{-}CH_2NO_2$$

Aq. NaN_3 added to a soln of β-nitrostyrene in glacial acetic acid, and allowed to react at room temp. → β-nitro-α-phenyl-α-azidoaethane. Y: 69%. F. e. s. J. H. Boyer, Am. Soc. *73*, 5248 (1951); cf. S. N. Ege and K. W. Sherk, Am. Soc. *75*, 354 (1953).

Acetic acid CH_3COOH

N-Cyanoethylation $NH \rightarrow NCH_2CH_2CN$

s. *8*, 405; of prim. ar. amines, also in the presence of CuCl and other inorganic catalysts, s. J. T. Braunholtz and F. G. Mann, Soc. *1953*, 1817

Hydrazoic acid HN_3

Schmidt reaction ←
Carboxylic acid amides from ketones

s. *1*, 362; α-acylaminocarboxylic acid esters s. D. O. Holland and J. H. C. Nayler, Soc. *1953*, 280

Oxygen O_2

2-Nitronitric acid esters from ethylene derivatives $C{:}C \rightarrow C(NO_2)C(ONO_2)$

s. *3*, 279; steroid derivatives s. C. E. Anagnostopoulos and L. F. Fieser, Am. Soc. *76*, 532 (1954)

Sulfuric acid *H_2SO_4*

Amines from ethylene derivatives and nitriles via acylamines C:C → CHC(NH_2)

416. $CH_3[CH_2]_7CH{=}CH[CH_2]_7COOH + CH_3CN \rightarrow CH_3[CH_2]_xCH(NHCOCH_3)[CH_2]_yCOOH$ ($x+y=15$) $\rightarrow CH_3[CH_2]_xCH(NH_2)[CH_2]_yCOOH$

A vigorously stirred mixture of oleic acid and acetonitrile added during 35 min. at 27-30° to 95-H_2SO_4, and the product isolated 15 min. after the addition is complete → acetamidostearic acid (Y: 99%) refluxed 6 days with aq. 50%-H_2SO_4 → aminostearic acid sulfate (Y: 93%) dissolved in excess aq. NaOH to pH 12, then stirred and carefully neutralized with dil. aq. HCl to pH 5-6 → aminostearic acid (Y: 80%). F. e. of the first step, also modified procedure, s. E. T. Roe and D. Swern, Am. Soc. *75*, 5479 (1953).

Rearrangement

Oxygen/Carbon Type NC⌒OC

Sodium hydroxide *NaOH*

Acyl group migration OAc → NAc
N-Acyl from O-acyl

s. *5*, 261; s. a. J. A. Moore et al., Am. Soc. *76*, 2884 (1954)

Ureidocarboxylic acids from hydantoins C

s. *9*, 568

Potassium carbonate *K_2CO_3*

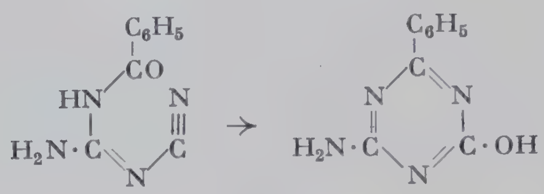
as used for determination of configuration

s. *9*, 246

n-Butylammonium carboxylate ←

1,3,5-Triazines from acyldicyanodiamides ○

417.



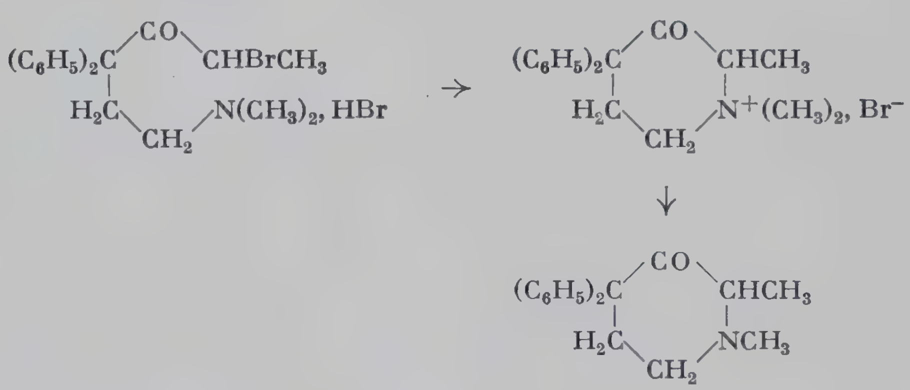
A soln. of benzoyldicyanodiamide (prepn. s. 511) in 37.5%-Cellosolve containing n-butylammonium salicylate or acetate refluxed ca. 8 min. → benzoguanide. Y: 84%. F. e., without catalyst, s. P. Adams et al., J. Org. Chem. *17*, 1162 (1952).

Halogen/Carbon Type NC ∩ HalC

Sodium hydrogen carbonate *$NaHCO_3$*

Piperidones from halogenaminoketones via piperidonium salts ○

418.



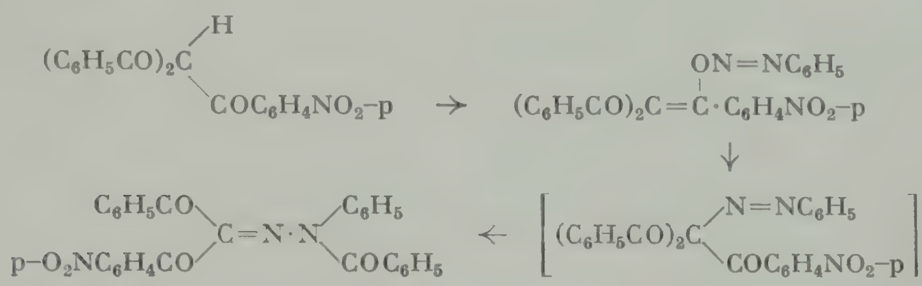
5-Bromo-1-dimethylamino-3,3-diphenyl-4-hexanone hydrobromide dissolved in 50%-ethanol, an equal volume of ether added, neutralized with $NaHCO_3$-soln. in the cold, shaken, and the ether layer separated quickly → 1,1,2-trimethyl-4,4-diphenyl-3-piperidonium bromide (Y: 95%) distilled in vacuo → 1,2-dimethyl-4,4-diphenyl-3-piperidone (Y: 78.7%). F. e. s. N. R. Easton et al., Am. Soc. *75*, 2086 (1953); s. a. F. F. Blicke and J. Krapcho, Am. Soc. *74*, 4001 (1952).

Carbon/Carbon Type NC⤵CC

Without additional reagents *w.a.r.*

Hydrazones via O-azo compounds ←

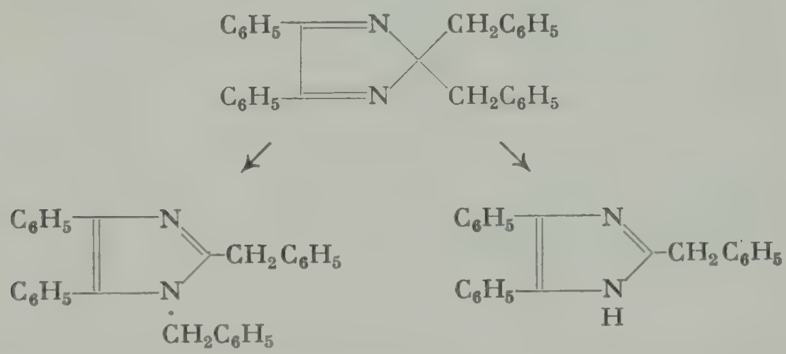
419.



p-Nitrotribenzoylmethane in ethyl acetate treated 45-90 min. with 2 moles K_2CO_3, the resulting K-salt extracted with cold water, then coupled with benzenediazonium chloride → O-phenylazo-p-nitrotribenzoylmethane (Y: 85%) heated 6 hrs. at 120° → p-nitrophenyl phenyl triketone benzoylphenylhydrazone (Y: 84%). F. e. s. D. Y. Curtin and C. S. Russell, Am. Soc. *73*, 5160 (1951).

Imidazoles from isoimidazoles, also with hydrolysis ←

420.



2,2-Dibenzyl-4,5-diphenylisoimidazole hydrate (prepn. s. 462)

heated 0.5 hr. at 250° in an oil bath → crude 1.2-dibenzyl-4.5-diphenylimidazole. Y: 67%.

dissolved in methanol containing HCl, and refluxed 0.5 hr. → crude 2-benzyl-4,5-diphenylimidazole. Y: ca. 100%.

F. e. s. M. Weiss, Am. Soc. *74*, 5193 (1952).

Hypobromite *BrO⁻*

tert-Carbinamines $R_3C \cdot NH_2$

s. *6*, 381; also further method s. K. E. Hamlin and M. Freifelder, Am. Soc. *75*, 369 (1953)

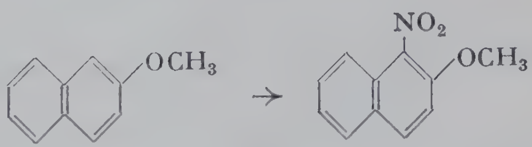
Exchange

Hydrogen ↑ NC ⇅ H

Without additional reagents *w.a.r.*

Reactions of nitrogen dioxide with ethers ←
Nitration

421.



N_2O_4 added at -10° to a soln. of 2-methoxynaphthalene in CCl_4, and the product isolated after 17 hrs. when the temp. has reached 15° → 1-nitro-2-methoxynaphthalene. Y: 96%. F. e. and reactions s. L. Horner and F. Hübenett, B. *85*, 804 (1952).

Sodium hydroxide *NaOH*

Arylazodisulfonylmethanes N:N

422. $C_6H_5NH_2 + CH_2(SO_2CH_3)_2 \rightarrow C_6H_5{-}N{=}N{-}CH(SO_2CH_3)_2$

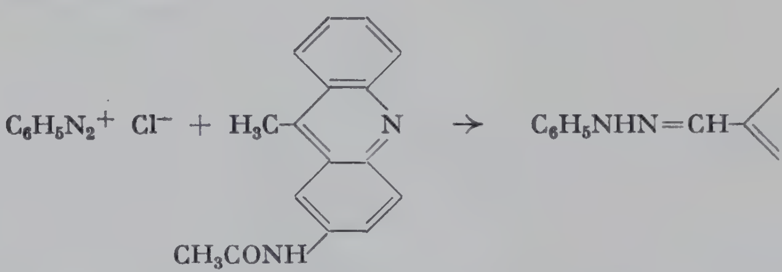
Aniline diazotized with aq. $NaNO_2$-ice water, satd. with Na-acetate, the Na-sulfate which is usually formed removed, cooled in ice-salt mixture, and bis(methylsulfonyl)methane in 2 *N* NaOH added → (phenylazo)-bis(methylsulfonyl)methane. Y: 56%. F. e. s. H. J. Backer, R. *70*, 733 (1951).

Azo compounds by coupling with simultaneous replacement of nitro by thiocyanato groups
s. *9*, 681

Sodium acetate *CH_3COONa*

Reaction of active methyl groups with diazonium salts ←

423.



Azo coupling is a useful method for determination of activity of H-atoms in methyl groups. Such activity is present in compounds con-

taining directly attached heterocyclic residues or ar. rings with electrophilic groups in o- and p-positions. Nucleophilic groups conjugated with the methyl group strongly reduce the activity of H-atoms in the latter. Transition of the hetero atom into the onium state enhances its electrophilic properties and increases the mobility of H-atoms in methyl groups conjugated with the hetero atom.—E: A soln. of benzenediazonium chloride (prepared from aniline with $NaNO_2$ in HCl at 0°) added in 2 portions over a period of 28 hrs. to a soln. of 2-acetamido-9-methylacridine and Na-acetate in acetic acid, and the product isolated after 24 hrs. → 2-acetamido-9-acridylaldehyde phenylhydrazone. Y: 65.9%. F. e. s. A. A. Kharkharov, Ж. *23*, 1175 (1953); C. A. *47*, 12390c.

Hydrazones from diazonium salts C
Hydrolytic ring opening

s. *7*, 406; also one-step procedure s. V. V. Feofilaktov, Sint. Org. *2*, 103 (1952); C. A. *48*, 666 g; s. a. Sint. Org. *2*, 98; C. A. *48*, 668 h

Sodium nitrite *$NaNO_2$*

Hydrazones from amines $NH_2 \rightarrow NHN{:}C$

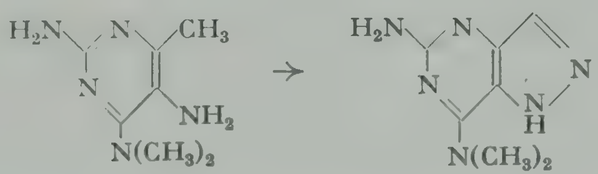
s. *3*, 290; s. a. V. V. Feofilaktov and N. K. Semenova, Sint. Org. *2*, 74 (1952); C. A. *48*, 592 d

Indazoles O

s. *1*, 321; s. a. H. R. Snyder and J. K. Williams. Am. Soc. *76*, 1298 (1954)

Ring closures with 5-aminopyrimidines O
1,2,4,6-Tetraazaindenes

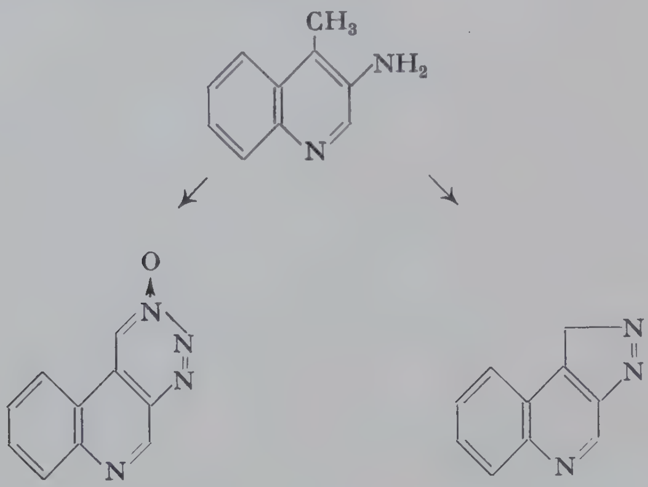
424.



4.2 g. 2.5-diamino-4-dimethylamino-6-methylpyrimidine diazotized with $NaNO_2$ in *N* HCl, then added to 3 *N* NaOH below 10°→4 g. 5-amino-7-dimethylamino-1,2,4,6-tetraazaindene. F. e., also by merely heating the diazonium salt soln., and other ring closures, s. F. L. Rose, Soc. *1952*, 3448.

1,2,3-Triazine and pyrazole rings

425.



3-Aminolepidine treated at 0° with aq. $NaNO_2$

in concd. HCl → 1,2,3,9-tetra-azaphenanthrene 3-oxide. Y: 84%.

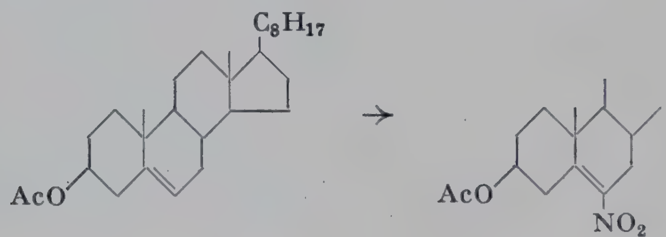
in 2 *N* H_2SO_4 → 3H-1,2,6-triaza-4,5-benzindene. 0.33 g. from 0.5 g.

F. e. s. D. W. Ockenden and K. Schofield, Soc. *1953*, 1915.

Potassium nitrite *KNO_2*

Nitration H → NO_2

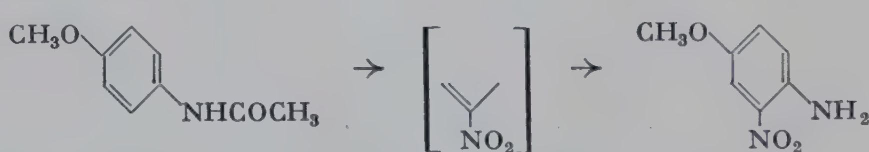
426.



Cholesteryl acetate added at 20° with rapid stirring to HNO_3 (d. 1.42), then K-nitrite added, and stirring continued 1 hr. → 3β-acetoxy-6-nitro-5-cholestene. Y: 80%. C. W. Shoppee and G. H. R. Summers, Soc. *1952*, 3361.

Potassium nitrate *KNO_3*

427.



Labeled compounds. A mixture of a slight excess of N^{15}-enriched KNO_3, H_2SO_4, and sufficient water to dissolve the salt, added to a soln. of acetyl-p-anisidine in acetic acid containing enough acetic anhydride to

convert the added water to acetic acid, and the product hyrolyzed → 4-methoxy-2-nitraniline. Y: 77%; 70% based on KNO_3.—When H_2SO_4 alone is used as solvent, or when the startg. m. is added to the nitrating mixture, the nitro group is introduced in the ortho position to the methoxyl group. A. H. Blatt and N. Gross, Am. Soc. *75*, 1245 (1953).

Pyridine *C_5H_5N*

Formazans from hydrazones C(=N·NH·)(N=N·)

s. *8*, 421; s. a. J. N. Ashley et al., Soc. *1953*, 3881

Cupric nitrate *$Cu(NO_3)_2$*

Nitration **H → NO_2**

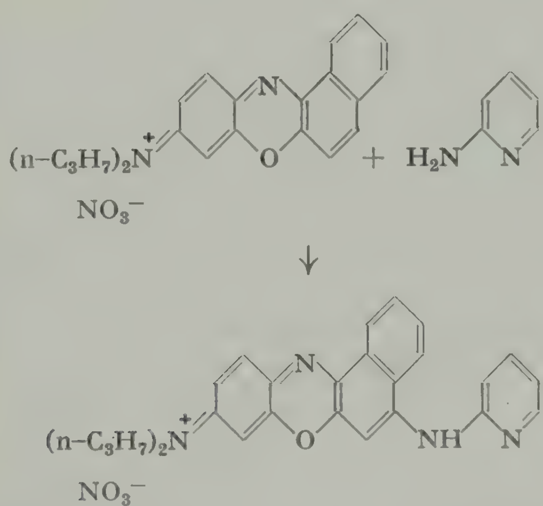
cf. Synth. Meth. *6*, 386.

428. The Cu-nitrate reagent seems to have certain advantages in nitrating organosilanes, possibly because it affords a relatively non-acidic nitrating medium. R. A. Benkeser and P. E. Brumfield, Am. Soc. *73*, 4770 (1951).

Nitrates/oxygen ←

Amination **H → N<**

429.



2-Aminopyridine added to a soln. of 9-di-n-propylaminobenzo[a]phenoxazonium nitrate in ethanol, gently warmed a few min., then allowed to stand at room temp. in an open beaker for several days → 9-di-n-propylamino-5-(2-pyridylamino)benzo[a]phenoxazonium nitrate. Crude Y: 80%. (Am. Soc. *74*, 584.)—In some instances, aeration increases the yield and shortens the reaction time (Am. Soc. *74*, 578). F. e. s. M. L. Crossley et al., Am. Soc. *74*, 584, 578 (1952).

Sulfuric acid *H_2SO_4*

Nitration $H \rightarrow NO_2$
N-Oxides as intermediates

s. *6*, 389; s. a. E. C. Taylor, Jr., and A. J. Crovetti, J. Org. Chem. *19*, 1633 (1954)

Molybdenum trioxide-alumina *MoO_3-Al_2O_3*

Nitriles from hydrocarbons ←

s. *6*, 388; s. a. Ind. Eng. Chem. *45*, 282 (1953)

Via intermediates *v.i.*

Aminophenols from phenols via azophenols $H \rightarrow NH_2$

with aniline s. *5*, 267; with sulfanilic acid s. *1*, 173; H. E. Albert, Am. Soc. *76*, 4985 (1954)

Oxygen ↑ NC⇅O

Without additional reagents *w.a.r.*

Glycosamines $OH \rightarrow NHR$

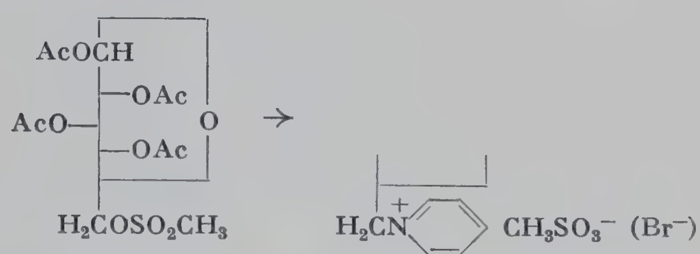
s. *7*, 416/7; *8*, 85; with aniline in abs. ethanol s. R. W. Jeanloz, Am. Soc. *76*, 5684 (1954); also with NH_3 s. F. Micheel et al., B. *85*, 1092 (1952)

α-Amino- from α-hydroxy-sulfones SO_2CH_2NHR

s. *8*, 426; s. a. H. Bredereck and E. Bäder, B. *87*, 129 (1954)

Quaternary ammonium salts ←
from sulfonic acid esters
Carbohydrate derivatives

430.



A soln. of 1,2,3,4-tetraacetyl-6-methanesulfonyl-β-D-glucose in anhydrous pyridine refluxed 2.5 hrs. → 1,2,3,4-tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose methanesulfonate (Y: 60%), 1 g. passed through a column containing Amberlite IRA-400 ion exchange resin which has been treated with dil. HBr soln. → 520 mg. 1,2,3,4-tetraacetyl-6-pyridinium-6-desoxy-β-D-glucose bromide. B. M. Iselin and J. C. Sowden, Am. Soc. *73*, 4984 (1951).

Aminomethylene from hydroxymethylene compounds C:C·OH → C:C·N<

s. *7*, 419; s. a. H. Davoll and F. B. Kipping, Soc. *1953*, 1395

α-Aminomethyleneketones from α-hydroxymethyleneketones

s. *2*, 725a; s. a. L. B. Barkley et al., Am. Soc. *76*, 5014 (1954)

Azomethines from amines and oxo compounds by azeotropic distillation $NH_2 + OC \rightarrow N{:}C$

s. *8*, 550; s. a. E. P. Goldberg and H. R. Nace, Am. Soc. *75*, 6260 (1953); R. B. Moffett, Org. Synth. *34*, 64 (1954)

Nitrones from hydroxylamines NHOH → N(O):C

s. *8*, 429; s. a. Am. Soc. *75*, 285 (1953)

Hydrazones CO → C:NNHR

s. *3*, 307; *9*, 121; s. a. C. L. Arens and R. J. Mesley, Soc. *1953*, 178; α-dihydrazones s. A. C. Cope, D. S. Smith, and R. J. Cotter, Org. Synth. *34*, 42 (1954)

Acylhydrazones

s. *5*, 273; s. a. H. L. Yale et al., Am. Soc. *75*, 1933 (1953)

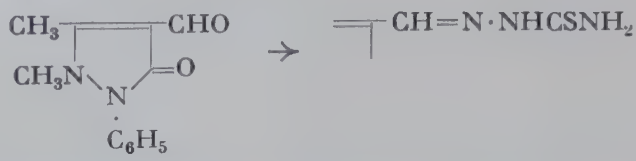
Resolution of racemic oxo compounds via acylhydrazones

431. $CONHNH_2$ + $OCHCH[CH_2]_3CHC_2H_5$ (with CH_3 on each marked C) → / ← $CONHN{=}CHCH[CH_2]_3CHC_2H_5$ (with CH_3 on each marked C)

$$\begin{array}{l} CONHNH_2 \\ HCOH \\ HOCH \\ CONH_2 \end{array} + \begin{array}{l} OCHCH[CH_2]_3CHC_2H_5 \\ \quad\;\; CH_3 \qquad\quad CH_3 \end{array} \rightleftarrows \begin{array}{l} CONHN{=}CHCH[CH_2]_3CHC_2H_5 \\ HCOH \qquad\quad CH_3 \qquad\quad CH_3 \\ HOCH \\ CONH_2 \end{array}$$

Methanol followed by 8.7 cc. rac-2,6-dimethyloctanal added to an aq. soln. of 7.5 g. D-tartramide acid hydrazide, allowed to stand overnight, the crude product recrystallized 2 times from alcohol → 7.5 g. 2,6-dimethyloctanal D-tartramazone, recrystallized a third time, and the first fraction (2.8 g.) hydrolyzed by gently heating with aq. H_2SO_4 on a water bath → 1.2 g. (+)-2,6-dimethyloctanal. Optical purity 92%.— The reagent is easily available. F. Nerdel and E. Henkel, B. *85*, 1138 (1952).

Thiosemicarbazones,
also by interchange CO → C:N·NHCSNH$_2$

432. 

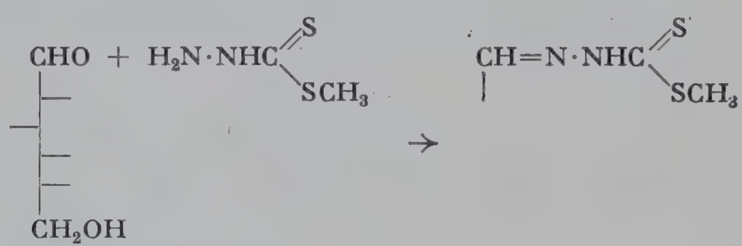
1-Phenyl-2,3-dimethyl-4-formyl-5-pyrazolone refluxed in alcohol

with thiosemicarbazide at 60° for 15 min. →	with acetone thiosemicarbazone for 3 hrs. →

1-phenyl-2,3-dimethyl-4-formyl-5-pyrazolone thiosemicarbazone.
Y: ca. 100%.

Also with thiosemicarbazide hydrochloride and Na-acetate in alcohol-water during 24 hrs. at room temp. in 92% yield, s. J. Ledrut and G. Combes, Bl. *1952*, 189; cf. T. S. Gardner et al., J. Org. Chem. *16*, 1121 (1951); W.L.Nobles and J.H.Burckhalter, J. Am. Pharm. Assoc. *42*, 176 (1953).

Dithiocarbalkoxyhydrazones
Carbohydrate derivatives CO → C:N·NHC(=S)SR

433. 

A mixture of 5.1 g. D-glucose and 3.4 g. dithiocarbomethoxyhydrazine (methyl dithiocarbazinate) refluxed 20 min. in methanol-water (1:1) → 7.7 g. N-dithiocarbomethoxy-N′-D-*gluco*-pentahydroxyhexylidenehydrazide. F. e., also with diacetyl, s. R. Hull, Soc. *1952*, 2959.

Formamides NCHO

s. *9*, 113

Acylation of amines NH → NAc

s. *9*, 392

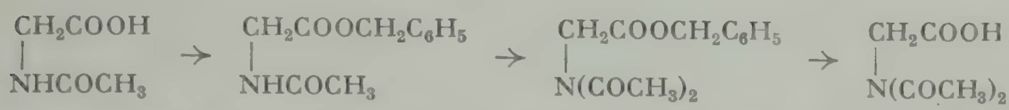
Carboxylic acid amides
from carboxylic acid esters COOR → CONHR

s. *7*, 425; *8*, 436; in toluene–1,2,4-trichlorobenzene s. J. Weijlard, G. Purdue, and M. Tishler, Am. Soc. *76*, 2505 (1954)

(Diacylamino)carboxylic acids from acylaminocarboxylic acids Protection of carboxyl groups by formation of benzyl esters

NHAc → $N(Ac)_2$

434.



A mixture of aceturic acid, benzyl alcohol, concd. H_2SO_4, and toluene refluxed 48 hrs. in a Soxhlet extraction apparatus containing anhydrous BaO in the thimble, the BaO being replaced by fresh oxide after 16 hrs. → benzyl aceturate (Y: 91.0%) dissolved in acetic anhydride, and refluxed 5 hrs. → N,N-diacetylglycine benzyl ester (Y: 91%) hydrogenated 3 hrs. with Pd-on-Darco in dry dioxane → crude N,N-diacetylglycine (Y: 97.2%). F. e. s. J. C. Sheehan and E. J. Corey, Am. Soc. *74*, 4555 (1952).

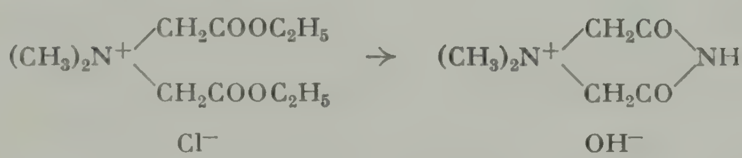
Dicarboxylic acid imides from dicarboxylic acids

○

s. *8*, 439; with NH_3 s. C. A. Miller and L. M. Long, Am. Soc. *75*, 6256 (1953); H. L. Lochte and E. N. Wheeler, Am. Soc. *76*, 5548 (1954)

Dicarboxylic acid imides from dicarboxylic acid esters

435.



Diethyl methyliminodiacetate methochloride added to a satd. anhydrous alc. NH_3 soln. → methyliminodiacetic acid imide methohydroxide. Y: 80-85%. M. Viscontini, J. Bally, and J. Meier, Helv. *35*, 451 (1952).

Dicarboxylic acid imides from dicarboxylic acid anhydrides

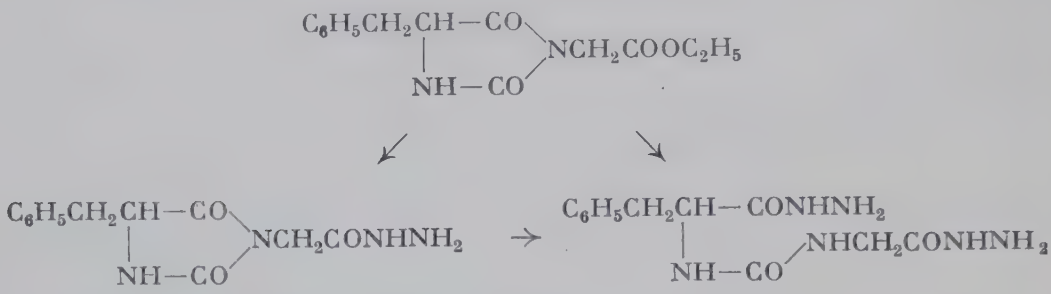
←

s. *5*, 341; s. a. L. M. Rice, E. E. Reid, and C. H. Grogan, J. Org. Chem. *19*, 884 (1954)

Carboxylic acid hydrazides from carboxylic acid esters

COOR → $CONHNH_2$

s. *7*, 426; *8*, 515; *9*, 476; with 85%-hydrazine hydrate s. a. H. L. Yale et al., Am. Soc. *75*, 1933 (1953); steroid derivatives, also with anhydrous hydrazine, s. L. F. Fieser and Wei-Yuan Huang, Am. Soc. *75*, 6306 (1953)

436. 

also with simultaneous hydantoin ring opening

2 moles hydrazine hydrate added to a soln. of ethyl 5-benzylhydantoin-3-acetate in warm abs. ethanol, and the precipitate, initially consisting of a mixture of the product with startg. m.. redissolved several times by warming → 5-benzylhydantoin-3-acetic acid hydrazide. Y: 80%.

Ethyl 5-benzylhydantoin-3-acetate or 5-benzylhydantoin-3-acetic acid hydrazide heated 3 hrs. with 5 moles hydrazine hydrate in abs. ethanol → carbonyl (glycine hydrazide) (DL-phenylalanine hydrazide). Y: 89%.

F. e. s. K. Schlögl, F. Wessely, and G. Korger, M. *83*, 493 (1952).

Diacylhydrazines AcNHNHAc

437. $$2\ (C_2H_5CO)_2O + H_2N{\cdot}NH_2 \rightarrow C_2H_5CONHNHCOC_2H_5$$

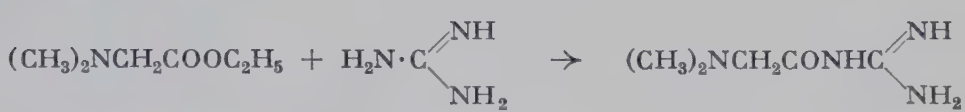
2 moles of propionic anhydride added slowly with cooling to 1 mole 85%-hydrazine hydrate soln., then heated slowly, and refluxed 1 hr. → dipropionylhydrazine. Y: 80%. F. e. s. Du-Yung Wu and R. M. Herbst, J. Org. Chem. *17*, 1216 (1952).

N,N′-Dicarbamylformamidines RNHCON:CH·NHCONHR

438. $$2\ C_6H_{11}NHCONH_2 + HC(OC_2H_5)_3 \rightarrow C_6H_{11}NHCON{=}CH{-}NHCONHC_6H_{11}$$

A mixture of cyclohexylurea and excess ethyl orthoformate refluxed 12 hrs. → N,N′-bis(cyclohexylcarbamyl)formamidine. Y: 82.3%. F. e. s. C. W. Whitehead, Am. Soc. *75*, 671 (1953).

Acylguanidines ←

439. 

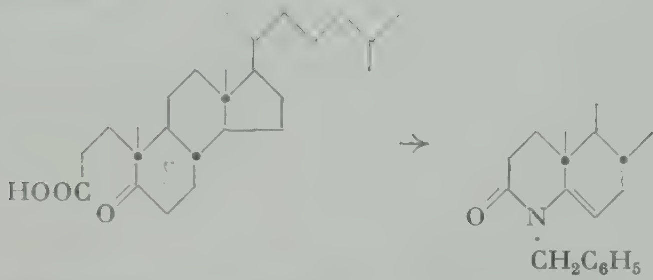
A soln. of guanidine hydrochloride in abs. alcohol treated with the calculated amount of a soln. of Na in alcohol, the resulting NaCl removed by centrifugation, then the soln. treated with N-dimethylglycine ethyl ester, and refluxed 5 min. → (N,N-dimethylglycyl)guanidine. Y: 65-70%. M. Viscontini, J. Bally, and J. Meier, Helv. *35*, 451 (1952).

Replacement of cyclic oxygen by cyclic nitrogen ←
2-Pyridones from 2-pyrones

s. 3, 302; limitations s. R. H. Wiley, P. Beasley, and L. H. Knabeschuh, Am. Soc. *76*, 311 (1954); s. a. *76*, 625

Enaminolactams from ketocarboxylic acids ○

440.



The ketoacid derived from cholestenone and benzylamine heated 1 hr. at 180° under N_2 → 4-benzyl-Δ^5-4-azacholestenone-3. Y: 99%. F. e. s. R. B. Woodward et al., Am. Soc. *74*, 4223 (1952).

Reactions with azeotropic water separation
(1,3-Di-N)-heterocyclics

s. *6*, 405; s. a. H. Zahn, H. Wilhelm, and A. Räuchle, A. *579*, 14 (1953)

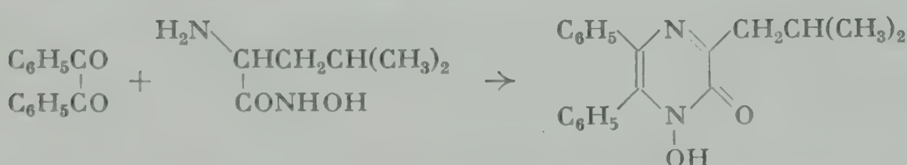
3,5-Piperazinediones

441.

A mixture of methyliminodiacetic acid and urea heated to ca. 160° until frothing starts, and the temp. raised to 170° during 1 hr. after the gas evolution has subsided → 1-methyl-3,5-piperazinedione. Y: 87%. Also labeled compounds s. B. H. Chase and A. M. Downes, Soc. *1953*, 3874.

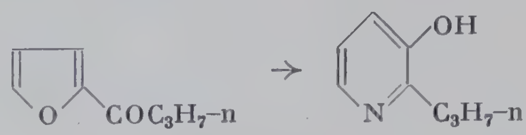
1-Hydroxy-2-pyrazinones from hydroxamic acids

442.



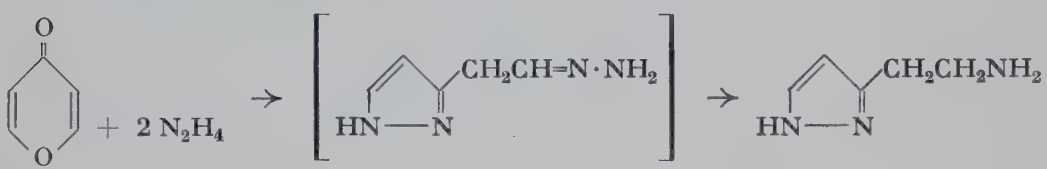
A mixture of benzil, L-leucinehydroxamic acid, and 50%-ethanol refluxed 17 hrs. → 1-hydroxy-2-keto-3-isobutyl-5,6-diphenyl-1,2-dihydropyrazine. Y: 67%. F. e. s. S. R. Safir and J. H. Williams, J. Org. Chem. *17*, 1298 (1952).

Pyridine ring from furan ring
3-Hydroxypyridines
Ring expansion ←

443. 

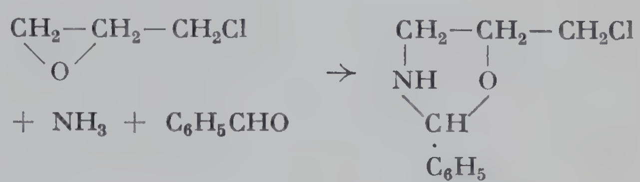
2-n-Butyrylfuran heated 20 hrs. at 165° with 2-3 moles alc. NH_3 in a sealed tube → 3-hydroxy-2-n-propylpyridine. Y: 74%. F. e. s. W. Gruber, Can. J. Chem. *31*, 564 (1953); f. intermediate formulas s. Synth. Meth. *8*, 469.

Pyrazoles from O-heterocyclics
Amines from hydrazones ←

444. 

A soln. of γ-pyrone in methanol added dropwise with stirring and cooling at ca. 25° to a soln. of hydrazine hydrate in methanol, when the exothermic reaction is over heated a few min. on a steam bath, cooled, liq. NH_3 added cautiously with stirring, and hydrogenated 1-2 hrs. with Raney-Ni at 90° and 1500 lb. pressure → 3-β-aminoethylpyrazole. Y: 81%. F. e. s. R. G. Jones et al., Am. Soc. *75*, 4048 (1953); *76*, 3172 (1954).

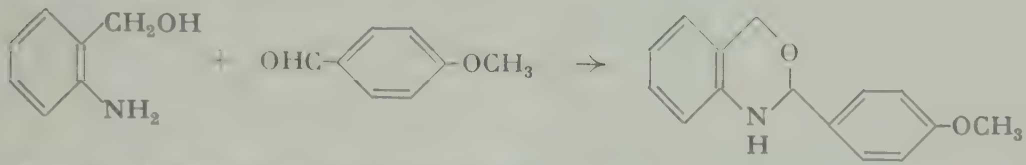
Oxazolidines
from oxido compounds ←

445. 

Aq. 29%-NH_3 added with stirring to a soln. of benzaldehyde in ethanol, then epichlorhydrin added in a thin stream with stirring, whereby the temp. rises to 40-45° over a period of 2 hrs., then allowed to stand overnight at room temp., finally heated 20 min. on a steam bath → 2-phenyl-5-chloromethyloxazolidine. Y: 69%. H. E. Carter and P. K. Bhattacharyya, Am. Soc. *75*, 2503 (1953).

Potassium hydroxide *KOH*

1,2-Dihydro-3,1-benzoxazines ○

446. 

A trace of KOH added to a soln. of o-aminobenzyl alcohol and anisaldehyde in alcohol. and warmed whereby the product precipitates → 1.2-dihydro-2-(p-methoxyphenyl)-3,1,4a-benzoxazine. Y: ca. 100%. B. Witkop, J. P. Patrick, and H. M. Kissman, B. 85, 949 (1952).

Sodium/alcohol *NaOR'*

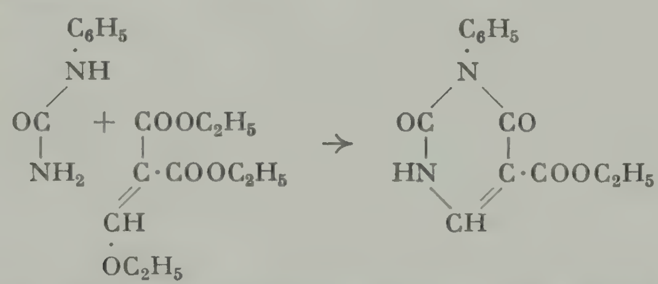
Hydroxamic acids from carboxylic acid esters COOR → CONHOH

s. *8*, 455; s. a. J. Org. Chem. *19*, 1140 (1954)

3,5-Pyrazolidiones from malonic acid esters ○

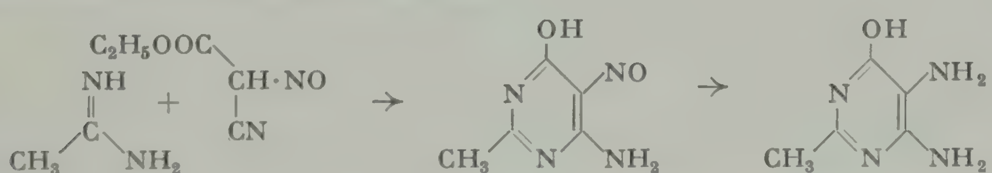
s. *7*, 439; s. a. J. Büchi et al., Helv. *36*, 75 (1953); method s. M. Conrad and A. Zart, B. *39*, 2282 (1906)

5-Carbethoxyuracils

447. 

Phenylurea and diethyl ethoxymethylenemalonate added to a soln. of Na in abs. ethanol, and allowed to stand 3 days at room temp. → 3-phenyl-5-carbethoxyuracil. Y: 88%. F. e. s. C. W. Whitehead, Am. Soc. *74*, 4267 (1952).

5-Amino- via 5-nitroso-pyrimidines

448. 

Acetamidine hydrochloride condensed with ethyl hydroxyiminocyanoacetate by using a soln. of Na in ethanol, the resulting Na-salt of 4-

amino-6-hydroxy-2-methyl-5-nitrosopyrimidine (Y: 79%) dissolved in water, warmed to 70°, wet Raney-Ni added portionwise until no further color change occurs, finally heated 1 hr. on a steam bath → 4,5-diamino-6-hydroxy-2-methylpyrimidine (Y: 72%). F. e. s. P. D. Landauer and H. N. Rydon, Soc. *1953*, 3721.

Sodium carbonate *Na_2CO_3*

Oximes from ketones CO → C:NOH

s. *9*, 36

Potassium carbonate *K_2CO_3*

Enamines from aldehydes CHCHO → C:CH(N<)

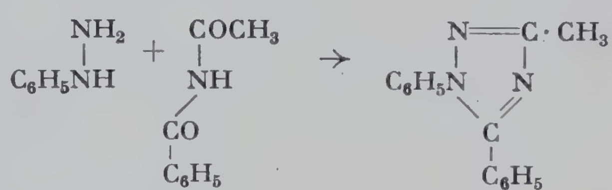
s. *2*, 380; s. a. R. Grewe et al., A. *581*, 85 (1953)

Sodium acetate *CH_3COONa*

Thiosemicarbazones CO → C:N·NHCSNH$_2$

s. *9*, 432

1,2,4-Triazoles from hydrazines ○
Einhorn-Brunner ring closure

449. 

Phenylhydrazine hydrochloride, N-acetylbenzamide, glacial acetic acid, and anhydrous Na- acetate refluxed 10 hrs. → 3-methyl-1,5-diphenyl-1,2,4-triazole. Y: 78%. F. e. s. M. R. Atkinson and J. B. Polya, Soc. *1952*, 3418.

Sodium hydrogen sulfite *$NaHSO_3$*

N-Acylation with peroxycarboxylic acids NH → NAc

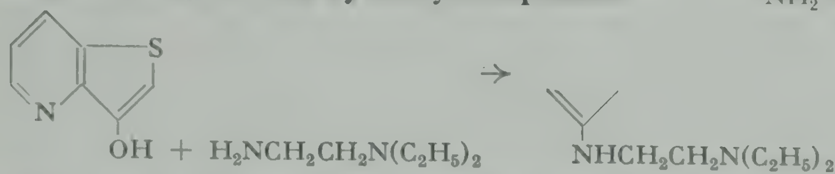
450. $CH_3COO_2H \rightarrow H_2NC_6H_5 \rightarrow CH_3CONHC_6H_5$

Aq. peracetic acid reduced with 10% excess aq. $NaHSO_3$-soln., cooled in an ice-bath, excess aniline added with swirling, and allowed to stand 1 hr. at room temp. → acetanilide. Y: 86%. F. e. and limitations s. A. H. Soloway and S. L. Friess, Am. Soc. *73*, 5000 (1951).

Potassium iodide *KI*

Sec. from prim. amines and hydroxy compounds $NH_2 \rightarrow NHR$

451.



A mixture of 3-hydroxythieno(3.2-b)pyridine, diethylaminoethylamine, and a little KI heated 72 hrs. at 170-180° in a sealed tube → 3-(diethylaminoethylamino)thieno(3,2-b)pyridine. Y: 58.5%. F e. s. J. T. Sheehan, Am. Soc. *74*, 5504 (1952).

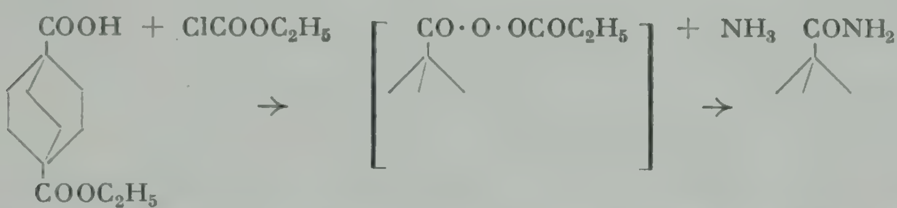
Trialkylamine *R_3N*

Carboxylic acid amides from carboxylic acids via mixed alkoxyformic acid anhydrides CON<

peptides s. 7, 447; s. a. B. F. Erlanger, H. Sachs, and E. Brand, Am. Soc. *76*, 1806 (1954); penicillin derivatives s. R. L. Barnden et al., Soc. *1953*, 3733

Triethylamine *$(C_2H_5)_3N$*

452.



Dicarboxylic acid amide esters. Ethyl chloroformate added rapidly with continuous agitation to an ice-salt cooled soln. of ethyl hydrogen bicyclo[2.2.2]octane-1,4-dicarboxylate and triethylamine in chloroform, after 15 min. anhydrous NH_3 passed through for 5 min., removed from the cooling bath, stirred 1 hr. at room temp., and allowed to stand overnight → ethyl 4-carboxamidobicyclo[2.2.2]octane-1-carboxylate. Y: 87%. J. D. Roberts, W. T. Moreland, Jr., and W. Frazer, Am. Soc. *75*, 637 (1953).

Peptides and carboxylic acid esters via mixed carboxylic acid anhydrides

453. $C_6H_5CH_2OCONHCH_2COOH + ClCOC_5H_{11}\text{-}i$

$\downarrow$

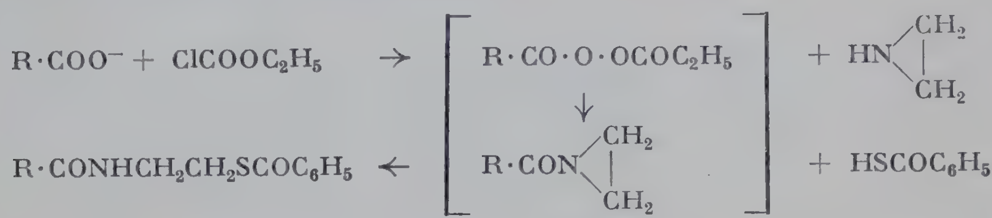
$[C_6H_5CH_2OCONHCH_2CO\cdot O\cdot OC\cdot C_5H_{11}\text{-}i]$ $+ C_6H_5CH_2CH(NH_2)COOC_2H_5 \rightarrow C_6H_5CH_2OCONHCH_2CO\text{-}NH\text{-}CH(CH_2C_6H_5)COOC_2H_5$

Peptides and carboxylic acid esters. A soln. of carbobenzoxyglycine and triethylamine in dry toluene cooled to 0° and isovaleryl chloride

added, then ethyl DL-phenylalaninate added to the resulting carbobenzoxyglycyl-isovaleric acid anhydride soln. and kept overnight at 8° → ethyl carbobenzoxyglycyl-DL-phenylalaninate. Y: 86%.—Anhydrides with isovaleric acid have been found particularly advantageous. F. e. s. J. R. Vaughan and R. L. Osato, Am. Soc. *73*, 5553 (1951); carboxylic acid esters s. E. D. Nicolaides, R. D. Westland, and E. L. Wittle, Am. Soc. *76*, 2887 (1954).

Carboxylic acid acylthioethylamides from carboxylic acids via mixed alkoxyformic acid anhydrides and carboxylic acid ethylenimides

454.



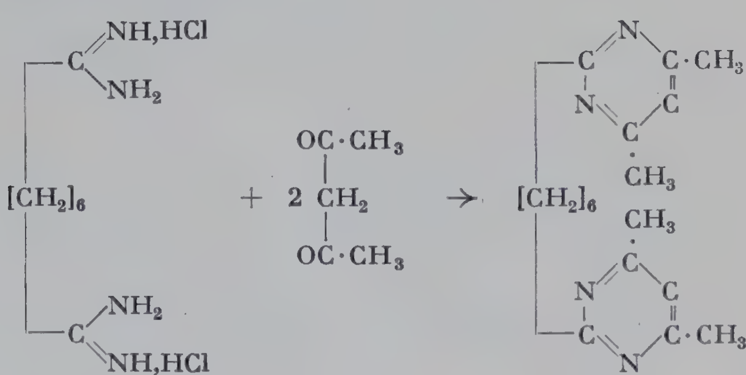
$HOCH_2C(CH_3)_2CH(OH)CONHCH_2CH_2\cdot = R$

Ethyl chloroformate in ethyl acetate added dropwise at −5° to a soln. of triethylammonium pantothenate (prepared from (+)-Ca-pantothenate and triethylamine in water) in dimethylformamide, after 10 min. dropped rapidly with stirring into a soln. of ethylenimine and triethylamine in ethyl acetate, after 20 min. poured into a soln. of thiobenzoic acid in ethyl acetate, and the product isolated after 30 min. at 0° → (+)-S-benzoylpantetheine. Y: ca. 50%. F. e. s. R. Schwyzer, Helv. *35*, 1903 (1952).

Piperidine *$C_5H_{11}N$*

Pyrimidines from amidines ○

455.



Suberodiamidine dihydrochloride, acetylacetone, and piperidine in pyridine refluxed 3 hrs. → hexamethylenebis-2-(4,6-dimethylpyrimidine). Y: 70%. F. e. s. D. D. Libman, D. L. Pain, and R. Slack, Soc. *1952*, 2305.

Pyridine/phosphorus trichloride *C_5H_5N/PCl_3*
s. Phosphorus trichloride/pyridine

Silver acetate *CH_3COOAg*

N-Acetylation NH → NAc
s. *9*, 876

Magnesium oxide *MgO*

Carboxylic acid amides from carboxylic acid chlorides COCl → CONHR

s. *5*, 341; s. a. R. E. Bowman and J. F. Cavalla, Soc. *1954*, 1171

Alkylmagnesium iodide *RMgI*

Carboxylic acid amides from carboxylic acid esters
Bodroux reaction COOR → CON<

456. $C_6H_5NH_2 + CH_3MgI \rightarrow [C_6H_5NHMgI] + CH_3OOC{\cdot}C_5H_{11} \rightarrow C_6H_5NHCOC_5H_{11}$

2 moles aniline in dry ether added slowly to 2 moles methyl-MgI in ether, after the vigorous reaction has subsided, methyl hexanoate in ether added, and refluxed 2 hrs. on a water bath → hexanoanilide. Y: 87%. F. e. s. H. L. Bassett and C. R. Thomas, Soc. *1954*, 1188.

Magnesium chloride *$MgCl_2$*

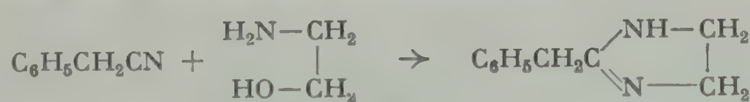
Tert. amines from oxo compounds
Extension of the Leuckart synthesis CO → $CHNR_2$

457. $$\underset{C_2H_5}{C_6H_5\dot{C}O} + HCON(CH_3)_2 \rightarrow \underset{C_2H_5}{C_6H_5\dot{C}HN(CH_3)_2}$$

A mixture of propiophenone, dimethylformamide, Mg-chloride hexahydrate, and 85%-formic acid heated with distillation of the volatile constituents until the pot temp. reaches approximately the boiling point of the formamide, then refluxed 8 hrs. with stirring → N,N-dimethyl-α-ethylbenzylamine. Conversion: 30%. Y: 79%. F. e., also with α,β-unsatd. carbonyl compounds, s. C. F. Bunnett, J. L. Marks, and H. Moe, Am. Soc. *75*, 985 (1953).

Zinc chloride/ammonium chloride *$ZnCl_2/NH_4Cl$*

Imidazolines from nitriles and aminoalcohols

458.


NH_4Cl suspended in a soln. of $ZnCl_2$ in benzyl cyanide, then monoethanolamine added dropwise with stirring during 30 min. at 210-220°,

and heating continued for 1.5 hrs. at the same temp. → 2-benzylimidazoline. Y: 66%. F. e., with lower yields, s. G. Kubiczek and L. Neugebauer, M. *80*, 815 (1949).

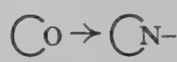
Aluminum *Al*

Amines from oxo compounds CO → CHNHR

459. $(CH_3)_3C\cdot COCH_3 + CH_3NH_2 \rightarrow (CH_3)_3C\cdot CH(NHCH_3)CH_3$

Aq. 30%-methylamine added to a soln. of pinacoline in alcohol, and this mixture added during 1 hr. with stirring and cooling to a suspension of Al (activated with Hg and $HgCl_2$) in 50%-alcohol → 2-methylamino-3,3-dimethylbutane. Y: 75-80%.—This method is convenient for laboratory preparations. F. e. s. H. Albers and S. Lange, B. *85*, 278 (1952); method s. Knoll A. G. and W. Klavehn, D. R. P. 617 536.

Aluminum oxide *Al_2O_3*

Replacement of cyclic oxygen by cyclic nitrogen 

s. *1*, 328; N-subst. piperidines s. A. N. Bourns, H. W. Embleton, and M. K. Hansuld, Org. Synth. *34*, 79 (1954)

Acetic anhydride *$(CH_3CO)_2O$*

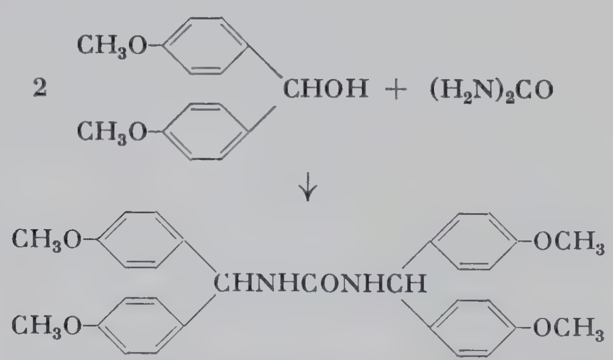
Formylation of amines $NH_2 \rightarrow NHCHO$

s. *2*, 391; s. a. J. Bornstein, W. J. Reid, and D. J. Torres, Am. Soc. *76*, 2760 (1954)

Formic acid *HCOOH*

Sym. ureas from alcohols and urea $(RNH)_2CO$

460.



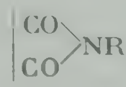
A soln. of 0.2 g. di-(p-methoxyphenyl)methanol in formic acid added to 0.06 g. urea in formic acid, and worked up after 20 min. → 0.2 g. bis-[di-(p-methoxyphenyl)methyl]urea. M. P. Balfe, J. Kenyon, and E. M. Thain, Soc. *1952*, 790.

Acetic acid *CH_3COOH*

Hydrazones C:O → C:NNH·

s. 2, 396/7: separation of ketosteroids by benzilic acid hydrazide s. L. Velluz et al., Bl. *1953*, 409

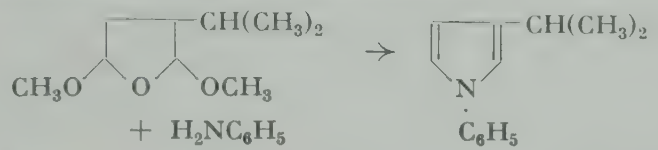
Phthalimides from amines



s. *1*, 331/2; s. a. C. M. Atkinson et al., Soc. *1954*, 2023

Pyrroles from 2,5-dialkoxytetrahydrofurans ←

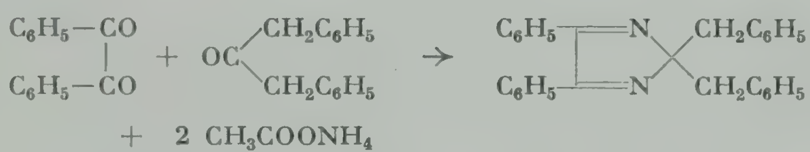
461.



A soln. of 2.5-dimethoxy-3-isopropyltetrahydrofuran and aniline in acetic acid refluxed 1.5 hrs. → crude 1-phenyl-3-isopropylpyrrole. Y: 83%. F. e. s. N. Elming and N. Clauson-Kaas, Acta Chem. Scand. *6*, 867 (1952).

Isoimidazoles

462.

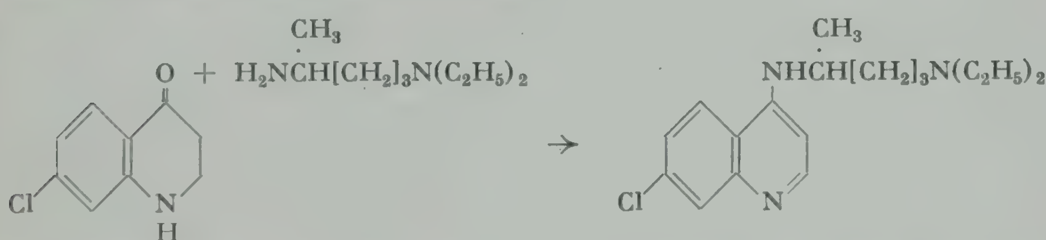


A mixture of dibenzyl ketone, benzil, NH_4-acetate, and acetic acid refluxed 1 hr. → 2,2-dibenzyl-4,5-diphenylisoimidazole hydrate (startg. m. f. 420). Y: 80%. M. Weiss, Am. Soc. *74*, 5193 (1952).

Nitrobenzene *$C_6H_5NO_2$*

N-Subst. 4-aminoquinolines from 4-keto-1,2,3,4-tetrahydroquinolines ←

463.



A mixture of 4-diethylamino-1-methylbutylamine, 4-keto-7-chloro-1,2,3,4-tetrahydroquinoline, and nitrobenzene heated 5 hrs. in an oil bath at 155-160° under N_2 → crude chloroquine. Y: 92%. F. e., also in phenol-nitrobenzene, s. W. S. Johnson and B. G. Buell, Am. Soc. *74*, 4513 (1952).

Hydrazoic acid HN_3

Nitriles from aldehydes CHO → CN

s. *4*, 380; s. a. W. E. McEwen, W. E. Conrad, and C. A. VanderWerf, Am. Soc. *74*, 1168 (1952)

Phosphorus pentoxide P_2O_5

Aminodesoxybenzoins from benzoins ←
Voigt reaction

s. *4*, 382; with heterocyclic sec. amines s. R. V. Heinzelmann and B. D. Aspergren, Am. Soc. *75*, 3409 (1953)

Tetraethyl pyrophosphite $(C_2H_5O)_2POP(OC_2H_5)_2$

Subst. carboxylic acid amides COOH → CON<
from carboxylic acids
Peptide synthesis

464.

$$C_6H_5CH_2OOCNHCH_2COOH + H_2N\underset{}{\overset{CH_2C_6H_5}{\dot{C}}}HCOOC_2H_5$$

$$\rightarrow C_6H_5CH_2OOCNHCH_2CONH\overset{CH_2C_6H_5}{\dot{C}}HCOOC_2H_5$$

Carbobenzoxyglycine and ethyl DL-phenylalaninate added to diethyl phosphite, then tetraethyl pyrophosphite added, and heated 15 min. on a steam bath → ethyl carbobenzoxyglycyl-DL-phenylalaninate. Y: 94%.—No racemization of optically active compounds has been observed when one of the reactants is an acylamino acid. F. e. s. G. W. Anderson, J. Blodinger, and A. D. Welcher, Am. Soc. *74*, 5309 (1952); carboxylic acid anilides s. Am. Soc. *74*, 5514; oxytocin synthesis s. V. du Vigneaud, Am. Soc. *76*, 3115 (1954).

Dialkyl chlorophosphate $(RO)_2POCl$

Alkylation of amines NH → NR

465. $$(C_6H_5)_2NH + (C_2H_5O)_2POCl \rightarrow (C_6H_5)_2NC_2H_5$$

Diphenylamine and diethyl chlorophosphate heated to 140-155° when a vigorous reaction occurs, and the product isolated after 45 min. at 155-165° → di(phenyl)ethylamine. Y: 82.7%. F. e. s. B. P. Lugovkin and B. A. Arbuzov, Ж. *22*, 2041 (1952); C. A. *47*, 9283h.

Phosphoric acid H_3PO_4

2,4-Dinitrophenylhydrazones CO → C:N·NHR

466. A H_3PO_4-ethanol soln. of 2,4-dinitrophenylhydrazine as reagent has been found to be indefinitely stable and avoids the use of the more reactive H_2SO_4. E. s. G. D. Johnson, Am. Soc. *73*, 5888 (1951).

Subst. carboxylic acid hydrazides from carboxylic acid esters COOR → CONHNHR

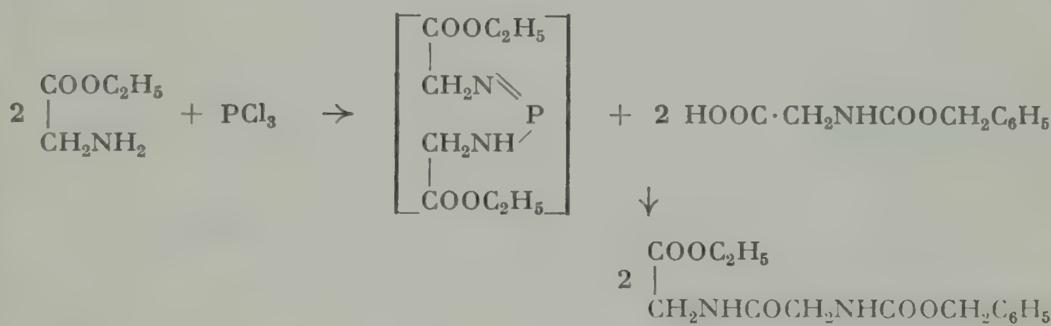
467. $$CH_3COOC_2H_5 + H_2N\cdot NHC_6H_5 \rightarrow CH_3CONHNHC_6H_5$$

Ethyl acetate, phenylhydrazine, and aq. H_3PO_4 gently refluxed for 1 hr. → β-acetylphenylhydrazine. Y: 60%.—Other methods were not successful. F. e. s. T. O. Jones, R. E. Halter, and W. L. Myers, Am. Soc. *75*, 6055 (1953).

Phosphorus trichloride/pyridine *PCl_3/C_5H_5N*

Carboxylic acid amides from carboxylic acids and phosphor compounds
Peptides COOH → CON<

468.



A soln. of PCl_3 in pyridine added to a soln. of glycine ethyl ester in pyridine, after 0.5 hr. heated 3 hrs. with N-carbobenzoxyglycine on a steam bath → N-carbobenzoxyglycylglycine ethyl ester. Y: 91%.—No racemization takes place in this process. F. e., also with isolation of the intermediate, s. Goldschmidt et al., A. *580*, 68 (1953); B. *86*, 1116 (1953).

Sulfuric acid *H_2SO_4*

N-Acylation NH → NAc

s. *5*, 302; s. a. J. R. E. Hoover and A. R. Day, Am. Soc. *76*, 4148 (1954)

Pyrimido[4,5-b]pyrazines ○

s. *1*, 345; *7*, 458; s. a. F. Korte, B. *87*, 1062 (1954)

Iodine *I*

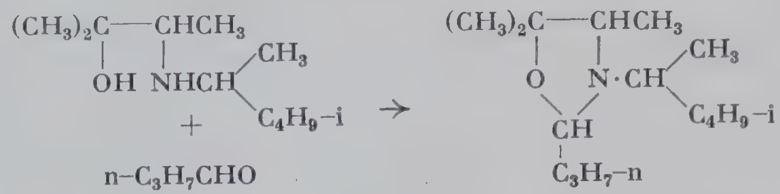
Sec. from prim. amines and phenols NH_2 → NHR

s. *9*, 713

Oxazolidines from 2-aminoalcohols

O

469.



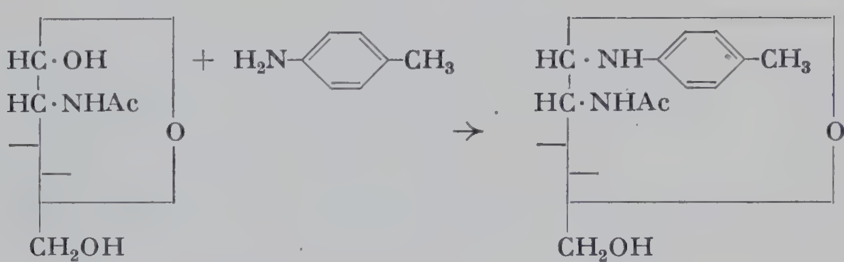
A mixture of equivalent amounts of 2-(α,γ-dimethylbutyl)amino-3-methyl-3-butanol and butyraldehyde with benzene azeotropically distilled in the presence of a trace of iodine until the theoretical quantity of water has been collected → 2-n-propyl-3-(α,γ-dimethylbutyl)-4,5,5-trimethyloxazolidine. Y: 80%. E. D. Bergmann, S. Pinchas, et al., Am. Soc. *73*, 5662 (1951); f. e. and limitations s. R. *71*, 168, 229, 237 (1952); Am. Soc. *75*, 358 (1953).

Ammonium chloride *NH_4Cl*

Glycosaminides

OH → N<

470.



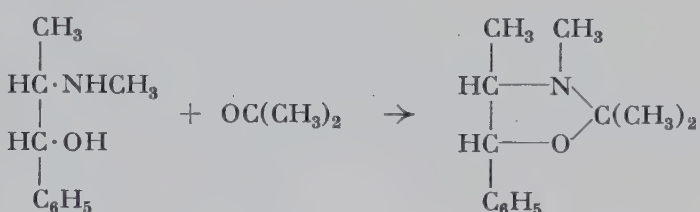
N-Acetylglucosamine, p-toluidine, and NH_4Cl in abs. methanol refluxed 4 hrs. → N-acetyl-D-glucosamine-p-toluidide. Y: 89%. F. e. s. A. Bertho and D. Koziollek, B. *87*, 934 (1954).

Hydrochlorides ←

Oxazolidines from 2-aminoalcohols

O

471.

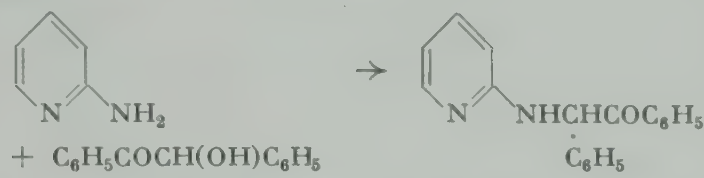


A soln. of l-ephedrine hydrate in acetone mixed with a soln. of l-ephedrine hydrochloride in abs. methanol, and refluxed 4 hrs. → acetone-l-ephedrine. Y: 90%. K. Freudenberg and J. Geiger, A. *575*, 145 (1952).

Hydrochloric acid *HCl*

Aminodesoxybenzoins from benzoins ←
Voigt reaction

472.



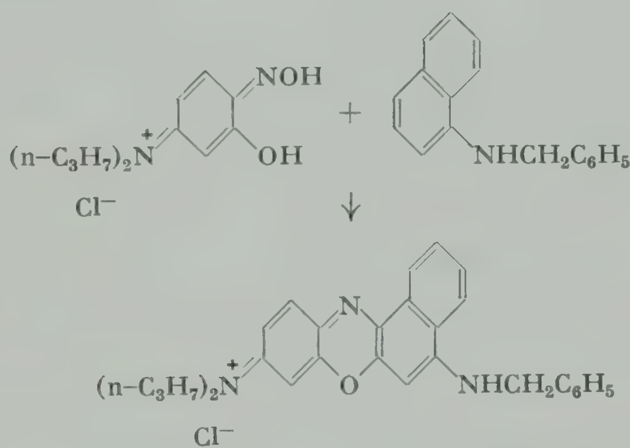
A mixture of benzoin, 2-aminopyridine, toluene, and concd. HCl refluxed 20 hrs. with a water separator → N-(2-pyridyl)desylamine. Y: 83%. I. A. Kaye, C. L. Parris, and W. J. Burlant, Am. Soc. *75*, 746 (1953); cf. Synth. Meth. *4*, 382.

2,4-Dinitrophenylhydrazones CO → C:N·NHR

s. *1*, 347/8; of carbohydrates s. L. M. White and G. E. Secor, Am. Soc. *75*, 6343 (1953)

Phenoxazine ring ○

473.



5-Di-n-propylamino-2-nitrosophenol hydrochloride and concd. HCl added to a suspension of 1-(N-benzyl)naphthylamine in ethanol, and refluxed 3 hrs. with stirring → 5-benzylamino-9-di-n-propylamino-benzo[a]phenoxazonium chloride. Y: 64%. F. e. and methods s. M. L. Crossley et al., Am. Soc. *74*, 573, 578, 584 (1952).

Pyrazine ring synthesis
Pyrimido[4,5-b]pyrazines

s. *4*, 400; s. a. B. J. Magerlein and D. J. Weisblat, Am. Soc. *76*, 3033 (1954)

Nickel *Ni*

Prim. amines from oxo compounds CO → $CHNH_2$

s. *3*, 350; s. a. D. G. Norton et al., J. Org. Chem. *19*, 1054 (1954)

Via intermediates *v.i.*

Sec. amines from oxo compounds via azomethines CO → CHNHR

s. *1*, 354; s. a. D. G. Norton et al., J. Org. Chem. *19*, 1054 (1954)

Subst. carboxylic acid amides from carboxylic acids via carboxylic acid chlorides COOH → COCl → CON<

s. *9*, 627

474. $$\underset{\displaystyle CH_2COOCH_3}{CH_3CHCOOH} \rightarrow \left[\underset{\displaystyle CH_2COOCH_3}{CH_3CHCOCl}\right] + H_2NC_6H_5 \rightarrow \underset{\displaystyle CH_2COOCH_3}{CH_3CHCONHC_6H_5}$$

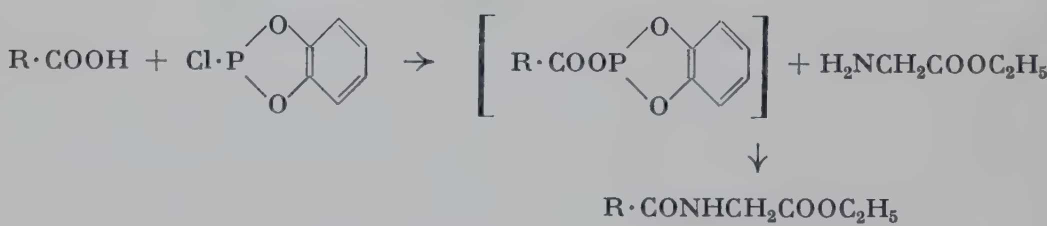
Mixed and partial dicarboxylic acid derivatives. — Avoidance of isomerization. A mixture of methyl β-carboxybutyrate, oxalyl chloride, and dry benzene warmed 3 hrs. at 30-40°, the solvent evaporated at 40°/12 mm, the product taken up in benzene, again evaporated, this operation repeated twice, then dissolved in dry ether, and carefully treated at 0° with aniline in the same solvent → methyl β-phenylcarbamylbutyrate. Y: 79%.—By this mild procedure, isomerization (cf. Synth. Meth. *8*, 188 is avoided. Also with the isomer s. J. E. H. Hancock and R. P. Linstead, Soc. *1953*, 3490.

Peptides

s. *5*, 316; s. a. D. Ben-Ishai, J. Org. Chem. *19*, 62 (1954)

Peptide synthesis with chlorophosphites COOH → CON<

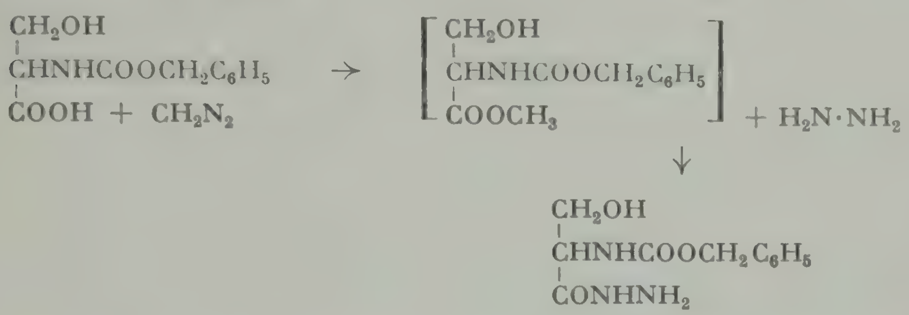
475.



$$R = \underset{\displaystyle CH_2C_6H_5}{C_6H_5CH_2OOCNHCH_2CONHCH-}$$

o-Phenylene chlorophosphite added to a soln. of carbobenzoxyglycyl-L-phenylalanine in benzene containing triethylamine, filtered, then refluxed 15 min. with ethyl glycinate → ethyl carbobenzoxyglycyl-L-phenylalanylglycinate. Y: 84%.—This procedure is simple, rapid, and gives good yields, with no apparent racemization of optically active derivatives. F. e. s. G. W. Anderson and R. W. Young, Am. Soc. *74*, 5307 (1952).

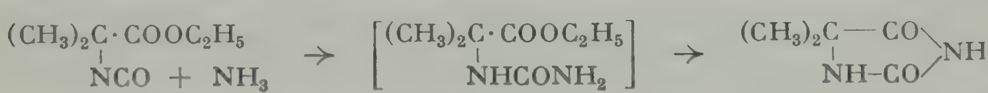
Carboxylic acid hydrazides from carboxylic acids COOH → $CONHNH_2$

476.


via carboxylic acid esters. Excess ethereal diazomethane added to a suspension of 15.3 g. carbobenzoxy-DL-serine in ethyl acetate, after dissolution of the amino acid evaporated in vacuo, dissolved in abs. ethanol, 85% hydrazine hydrate added, and allowed to stand overnight at room temp. → 14.9 g. carbobenzoxy-DL-serine hydrazide. E. A. Popenoe, D. G. Doherty, and K. P. Link, Am. Soc. *75*, 3469 (1953); *estimation of diazomethane* s. R. F. Raffauf, A. L. Farren, and G. E. Ullyot, Am. Soc. *75*, 2576 (1953); *relative reactivity of functional groups towards diazomethane*, -COOH 〉 COBr 〉 COCl 〉 OH 〉 $COCH_3$, s. A. J. Kosak, C. W. Huntington, and J. R. MacGregor, Am. Soc. *76*, 4481 (1954).

via carboxylic acid chlorides
s. *9*, 503

Hydantoins from α-isocyanatocarboxylic acid esters ○

477.


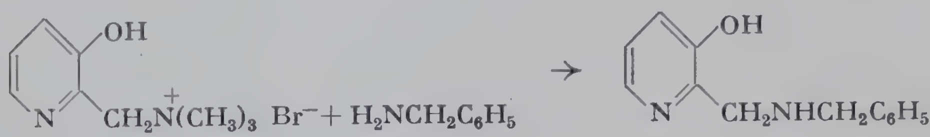
A mixture of ethyl α-isocyanatoisobutyrate and concd. NH_3 vigorously shaken, warmed 1 hr. at 60°, evaporated to dryness, then evaporated twice with aq. HCl to dryness → 5,5-dimethylhydantoin. Y: 86%. F.e.s. S. Goldschmidt and M. Wick, A. *575*, 217 (1952).

Nitrogen ↓ NC⇅N

Without additional reagents *w.a.r.*

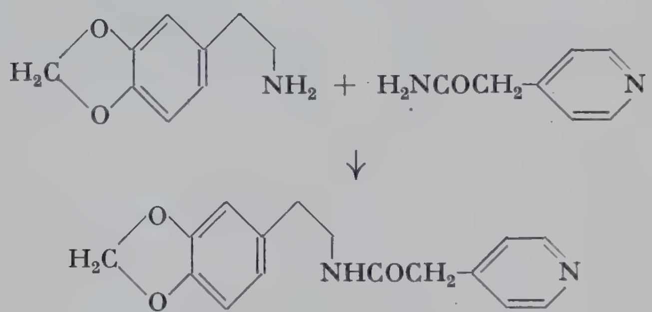
Sec. from prim. amines NH_2 → NHR
Exchange of substituents of pyrimido[4,5-b]pyrazines
s. *9*, 534

Sec. and tert. amines from quaternary ammonium salts by transamination NH → NR

478. 

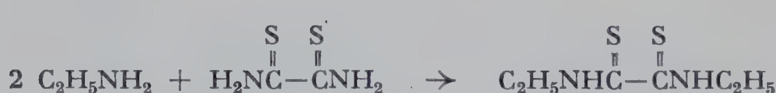
Benzylamine added to (3-hydroxy-2-pyridylmethyl)trimethylammonium bromide, then warmed 1.5 hrs. at 50° with stirring, and the product isolated as the dihydrochloride → 2-benzylaminomethyl-3-pyridol dihydrochloride. Y: 71%.—This reaction can be performed with amines which do not undergo the Mannich reaction or might react differently, as in the case of prim. amines. F. e. s. A. Stempel and J. A. Aeschlimann, Am. Soc. *74*, 3323 (1952).

Substitution of carboxylic acid amides $CONH_2$ → CONHR

479. 

Homopiperonylamine and 4-pyridylacetamide in tetralin heated 2 hrs. at 200° → N-(4-pyridylacetyl)homopiperonylamine. Y: 73%. C. R. Noller and E. A. Wunderlich, Am. Soc. *74*, 3835 (1952).

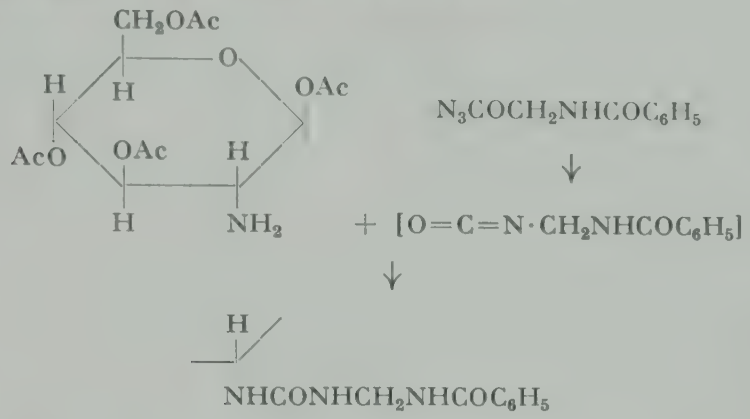
Substitution of carboxylic acid thioamides
Dithiooxamides $CSNH_2$ → CSNHR

480. 

A mixture of dithioöxamide and excess aq. 33%-ethylamine refluxed 15 min. on a water bath whereby a vigorous NH_3-evolution takes place after 10 min. → N,N′-diethyldithioöxamide. Y: 88%. F. e. s. H. M. Woodburn and C. E. Sroog, J. Org. Chem. *17*, 371 (1952).

Ureas from amines and carboxylic acid azides ←

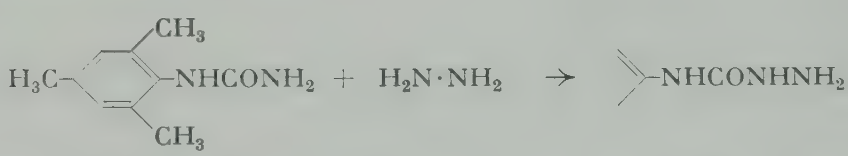
481.



Hippuryl azide added to a soln. of 1,3,4,6-tetraacetyl-β-D-glucosamine in ethyl acetate, and allowed to stand overnight at room temp. → N-(benzamidomethylcarbamyl)-1,3,4,6-tetraacetyl-β-D-glucosamine. Y: 73%.—No amide is obtained (cf. Synth. Meth. *6*, 226; *7*, 476/7), since the azide undergoes Curtius rearrangement before reacting with the amine. E. A. Popenoe, D. G. Doherty, and K. P. Link, Am. Soc. *75*, 3469 (1953); s. a. J. W. Hinman, E. L. Caron, and H. N. Christensen, Am. Soc. *72*, 1620 (1950).

Semicarbazides from ureas $NHCONH_2 \rightarrow NHCONHNH_2$

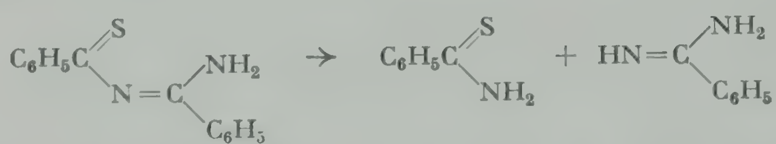
482.



Mesitylurea, a 50%-soln. of hydrazine hydrate, and ethanol refluxed until evolution of NH_3 ceases after ca. 72 hrs. → mesitylsemicarbazide. Y: 87%. J. Packer, J. Vaughan, and T. W. Watts, Soc. *1952*, 2654.

Cleavage of N-thioacylamidines ←
Diamidides

483.



N-Thiobenzoylbenzamidine dissolved in 2 *N* abs. ethanolic NH_3, and evaporated in vacuo after 30 min. → thiobenzamide (Y: 88%) and, after treatment with picric acid, benzamidinium picrate (Y: 74%). Also cleavage with amines, and with amidines to diamidides, ArC(:NH)N:C(NH_2)Ar, s. D. A. Peak, Soc. *1952*, 215.

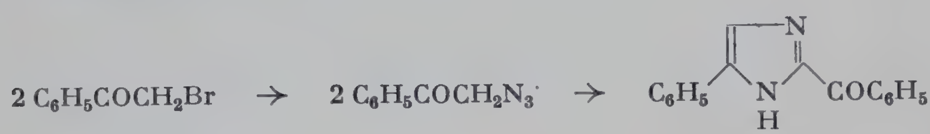
Amine salts of N-nitramines from N-nitrourethans ←

484. $$\underset{\textstyle NO_2}{(CH_3)_2CHN}COOC_2H_5 + 2\ C_6H_{11}NH_2 \rightarrow C_6H_{11}NHCOOC_2H_5 + \left[\underset{\textstyle NO_2}{(CH_3)_2CHN}\right]^- C_6H_{11}NH_3^+$$

Ethyl N-nitro-N-isopropylcarbamate (prepn. s. Am. Soc. *73*, 5043 (1951)) allowed to react with cyclohexylamine in ether → cyclohexylamine salt of isopropyl-N-nitramine (Y: 94.5%) and ethyl N-cyclohexylcarbamate (Y: 63%).—The salts may be used for the identification of amines and N-nitramines, and the reaction is also useful for the identification of N-nitrocarbamates. F. e. s. H. M. Curry and J. P. Mason, Am. Soc. *73*, 5041 (1951).

4-Subst. 2-acylimidazoles from α-halogenoketones via α-azidoketones ○

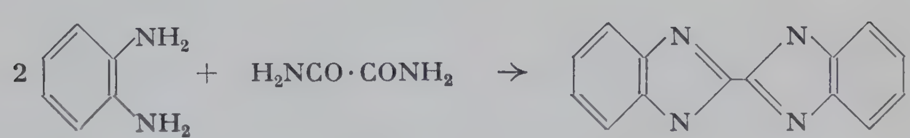
485.



A cold aq. soln. of NaN_3 added at 0-5° to a soln. of phenacyl bromide in ethanol and glacial acetic acid, and allowed to stand 24 hrs. in the refrigerator with intermittent shaking → phenacyl azide (Y: 93%) dissolved in trichlorobenzene, resorcinol dimethyl ether, or diphenyl ether, and heated between 180 and 240° for 30 min. or until no more N_2 and water vapor is evolved → 2-benzoyl-4(or 5)-phenylimidazole (Y: 64%). F. e. and limitation s. J. H. Boyer and D. Straw, Am. Soc. *74*, 4506 (1952).

Imidazole ring from carboxylic acid amides Bi(benzimidazoles)

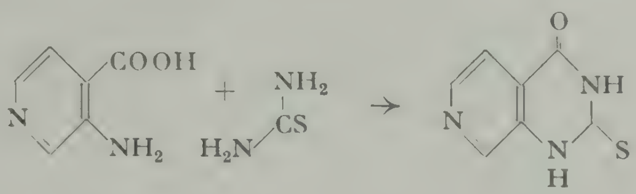
486.



4.4 g. oxamide, 10.8 g. o-phenylenediamine, and ethylene glycol refluxed 3 hrs. → 9.2 g. crude 2,2′-bi(benzimidazolyl). F. e. s. E. S. Lane, Soc. *1953*, 2238.

Copazolines

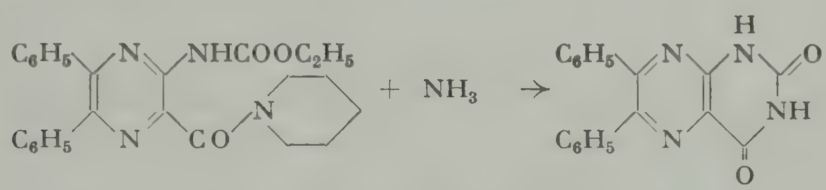
87.



A suspension of 15 g. 3-aminoisonicotinic acid and 12 g. thiourea in mineral oil heated 5 hrs. at 170-180° with stirring → 21 g. 2-thiocopazoline-2,4(1H,3H)dione. H. H. Fox, J. Org. Chem. *17*, 547 (1952).

Pyrimido[4,5-b]pyrazines from pyrazines

88.



A soln. of 3-carbethoxyamino-5,6-diphenylpyrazinoic acid piperidide in ethanol satd. with anhydrous NH_3, then heated 6 hrs. at 155° in a sealed tube → 6,7-diphenyllumazine. Y: 90%. F. methods s. E. C. Taylor, Jr., J. A. Carbon, and D. R. Hoff, Am. Soc. *75*, 1904 (1953).

Sodium hydroxide *NaOH*

Hydroxylamines from quaternary ammonium salts ←

s. *9*, 553

Nitrones from pyridinium salts ←
Kröhnke aldehyde synthesis
α-Ketoaldehydes from α-halogenoketones

s. *1*, 198/9; s. a. K. Balenović, D. Cerar, and L. Filipović, J. Org. Chem. *18*, 868 (1953)

Potassium hydroxide/alcohol *KOH*

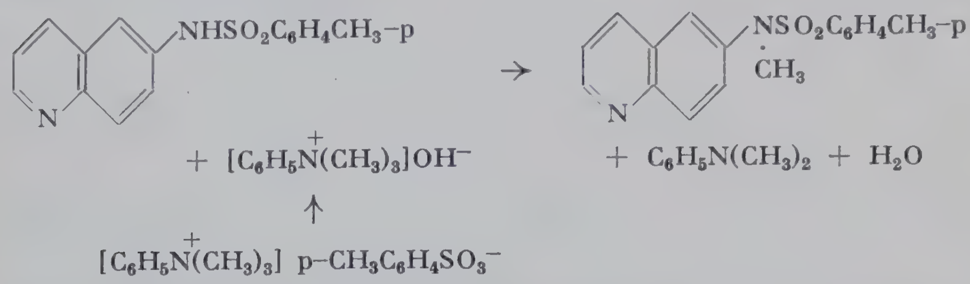
Replacement of nitro groups ←

s. *9*, 491

Sodium/alcohol *NaOR*

Selective N-alkylation NH → NR

489.



Trimethylphenylammonium p-toluenesulfonate added to a soln. of Na in alcohol, filtered, the filtrate mixed with 6-(p-tolylsulfonamido)quinoline, the ethanol distilled off, and the residue heated 50 min. at 107-112° with occasional stirring → 6-(N-methyl-p-tolylsulfonamido)quinoline. Y: 60%. A. M. Simonov, Ж. *22*, 2006 (1952); C. A. *47*, 9328g.

Phenyllithium *C_6H_5Li*

Diazo compounds from sulfonic acid azides $CH_2 \rightarrow CN_2$

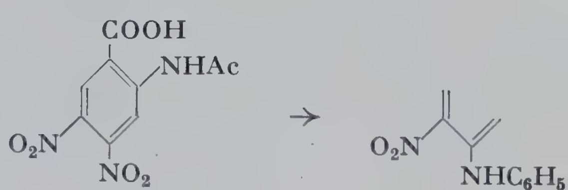
490.

A soln. of cyclopentadiene in ether added dropwise with stirring during 30 min. to a cooled soln. of phenyl-Li (from bromobenzene and Li), stirring continued for 1 hr. at room temp., forced under N_2-pressure in a slow, steady stream during 1 hr. into a cooled, stirred soln. of p-toluenesulfonyl azide in dry ether → diazocyclopentadiene (Y: 35%) and p-toluenesulfonamide (Y: 29%). W. von E. Doering and C. H. DePuy, Am. Soc. *75*, 5955 (1953).

Potassium carbonate *K_2CO_3*

Replacement of nitro groups ←

491.

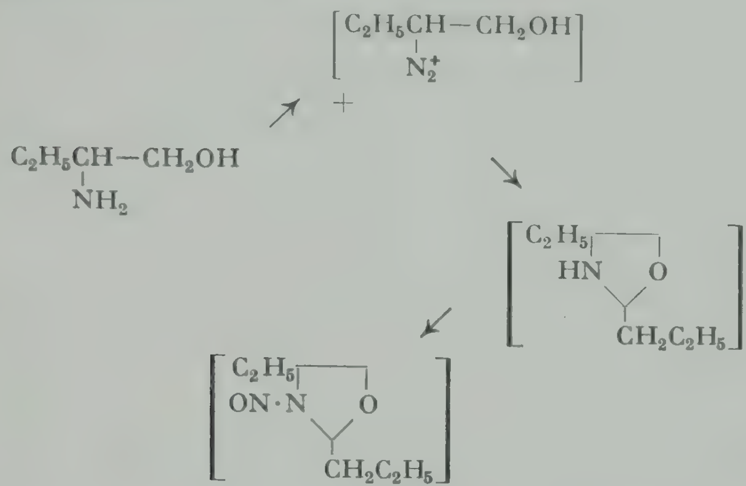


Partial replacement by amino groups. An intimate mixture of 4,5-dinitro-2-acetamidobenzoic acid and anhydrous K-carbonate added to aniline, and heated 30 min. on a steam bath → 5-nitro-4-anilino-2-acetamido-benzoic acid. Y: 92%. F. e. s. H. Goldstein and R. Jaunin, Helv. *34*, 1860 (1951); with KOH/alcohol s. Helv. *34*, 2222.

Sodium nitrite *$NaNO_2$*

3-Nitrosooxazolidines from 2 2-aminoalcohol molecules ○

492.



Aq. $NaNO_2$ added dropwise with stirring at 0-5° to a soln. of 2-amino-1-butanol in aq. acetic acid, stirring continued 1 hr. at the same temp., and overnight at room temp. → 2-propyl-4-ethyl-3-nitrosoöxazolidine. Y: 49-52%. H. R. Nace and M. H. Gollis, Am. Soc. *74*, 5189 (1952).

Copper *Cu*

α-Aminoketones from α-diazoketones $COCHN_2 \rightarrow COCH_2N<$

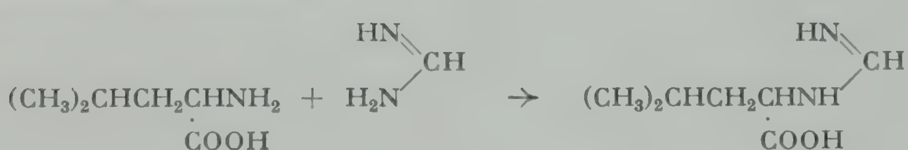
493.

Piperidine dissolved in abs. ethanol, the soln. stirred with Cu-bronze (Naturkupfer C) at 45°, a soln. of α-diazoacetophenone in abs. ethanol added slowly at a rate to maintain the temp. at 50° without external heating → α-(1-piperidyl)acetophenone. Y: 80%. P. Yates, Am. Soc. *74*, 5376 (1952).

Silver carbonate *Ag_2CO_3*

Substitution of amidines NH → NR

494.



Formamidine hydrochloride and Ag-carbonate added to a suspension of 1 g. L-leucine in formamide → 0.85 g. formimino-L-leucine. F. e. s. F. Micheel and W. Flitsch, A. *577*, 234 (1952).

Aluminum chloride *$AlCl_3$*

Azines from hydrazones $2\ R_2C{:}N{\cdot}NH_2 \rightarrow R_2C{:}N{\cdot}N{:}CR_2$

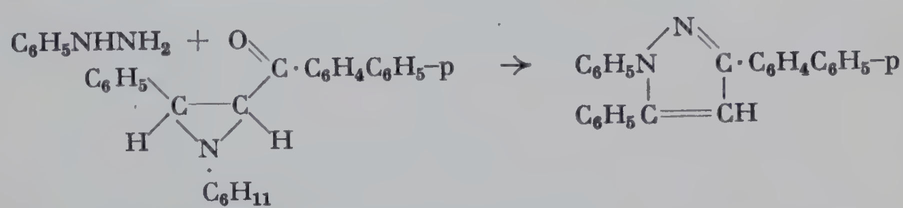
495. $$2\ (C_6H_5)_2C{=}N{\cdot}NH_2 \rightarrow (C_6H_5)_2C{=}N{\cdot}N{=}C(C_6H_5)_2$$

1 g. benzophenone hydrazone added all at once to boiling aq. $AlCl_3$. and heating continued until the product precipitates → 0.8 g. benzophenone azine. D. E. Pearson, K. N. Carter, and C. M. Greer. Am. Soc. *75*, 5905 (1953).

Acetic acid *CH_3COOH*

Pyrazoles from ethyleniminoketones ○

496.



cis-1-Cyclohexyl-2-phenyl-3-(p-phenylbenzoyl)ethylenimine warmed 15 min. at 40-50° in an ethanol-chloroform mixture containing glacial acetic acid and phenylhydrazine, until a clear soln. is obtained, then allowed to stand 12 hrs. at room temp. → 1,5-diphenyl-3-(p-xenyl)pyrazole. Y: 84%. F. e., pyrazolines from the *trans*-isomers, s. N. H. Cromwell and M. A. Graff, J. Org. Chem. *17*, 414 (1952).

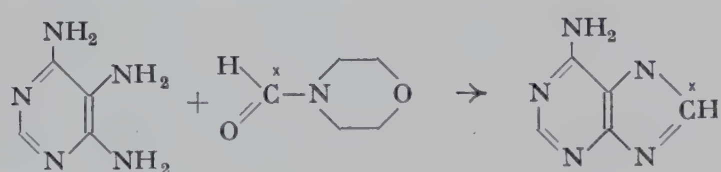
Isoalloxazines

s. *4*, 418; s. a. E. E. Haley and J. P. Lambooy, Am. Soc. *76*, 2926 (1954)

Sulfate ←

Labeled purines by transformylation

497.

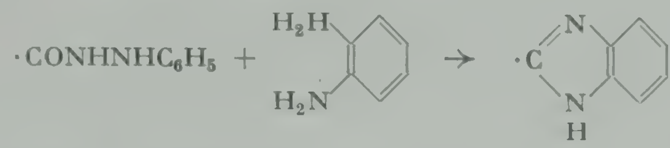


4,5,6-Triaminopyrimidine and N-formyl-C^{14}-morpholine heated 80 min. at 200° in a slow N_2-stream → adenine. Y: 92%. R. Abrams and L. Clark, Am. Soc. *73*, 4609 (1951).

Hydrochloric acid *HCl*

Benzimidazole derivatives in identification of carbohydrates

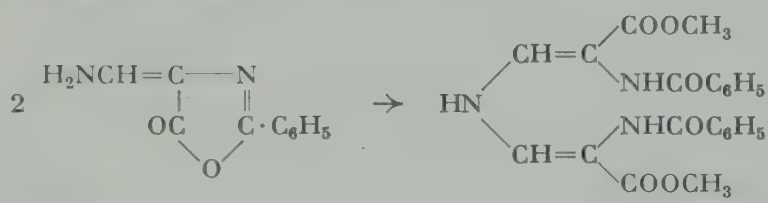
98.



7-Desoxy-L-*manno*-L-*gala*-heptonic phenylhydrazide allowed to react with o-phenylenediamine in the presence of HCl → 2-(L-*manno*-L-*gala*-*hepto*-1,2,3,4,5-pentahydroxyhexyl)benzimidazole. Y: 70%. Also from salts and lactones s. D. A. Rosenfeld et al., Am. Soc. *73*, 5907, 4907 (1951); method s. S. Moore and K. P. Link, J. Biol. Chem. *133*, 293 (1940).

Oxazolone ring opening with dimerization

99.



4 g. 4-aminomethylene-2-phenyl-5-oxazolone added to a soln. of dry HCl in methanol, and allowed to stand 5 days at 18-20° → 4 g. dimethyl β,β'-iminodi-(α-benzoylaminoacrylate). I. T. Strukov, Ж. *23*, 1344 (1953); C. A. *48*, 117b.

Via intermediates *v.i.*

Subst. carboxylic acid amides from carboxylic acid hydrazides via carboxylic acid azides Peptide synthesis $CONHNH_2 \rightarrow CONHR$

s. 7, 476/7; s. a. B. F. Erlanger, H. Sachs, and E. Brand, Am. Soc. *76*, 1806 (1954); E. Sondheimer and R. W. Holley, Am. Soc. *76*, 2816 (1954)

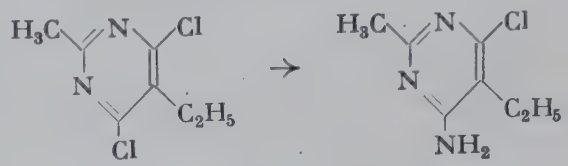
Halogen ↑ NC⇅Hal

Without additional reagents *w.a.r.*

Partial replacement of halogen by amino groups Hal → N<

s. 8, 497; s. a. E. A. Steck, R. P. Brundage, and L. T. Fletcher, Am. Soc. *76*, 3225 (1954); also sec. amines s. L. Katz and M. S. Cohen, J. Org. Chem. *19*, 767 (1954)

Exchange of substituents of pyrimidines

500. 

A mixture of 4,6-dichloro-5-ethyl-2-methylpyrimidine and concd. aq. NH_3 heated 9 hrs. at 132-140° in a sealed tube → 4-amino-6-chloro-5-ethyl-2-methylpyrimidine. Y: 88.9%.—At higher temp., both chloro substituents are replaced by amino groups. F. e. s. H. R. Henze, W. J. Clegg, and C. W. Smart, J. Org. Chem. *17*, 1320 (1952); s. a. G. B. Brown and V. Spicer Welicky, J. Biol. Chem. *204*, 1019 (1953).

2-Ethyleneamines from β,γ-ethylenehalides with subsequent N-acylation ←

501. $HOOC{\cdot}CH{=}CHCH_2Br \rightarrow [HOOC{\cdot}CH{=}CHCH_2NH_2] \rightarrow HOOC{\cdot}CH{=}CHCH_2NHCOCH_2C_6H_5$

A soln. of γ-bromocrotonic acid in liq. NH_3 allowed to evaporate slowly, water carefully added, evaporated to dryness on a steam bath, 2 equivalents of NaOH added, again evaporated to dryness, taken up in a little water, and treated with 1 equivalent of NaOH and 1 equivalent of phenylacetyl chloride with cooling and stirring → crude γ-phenylacetylaminocrotonic acid. Y: 83%.—Treatment with liq. NH_3 in dry dioxane was not successful. D. Todd and S. Teich, Am. Soc. *75*, 1895 (1953).

Sec. from prim. amines and halides Hal → NHR

s. *9*, 930; α-aminocarboxylic acid s. F. Blicke and P. E. Norris, Am. Soc. *76*, 3213 (1954)

Carboxylic acid amides from carboxylic acid chlorides Lower aliphatic amides COCl → $CONH_2$

502. $(C_2H_5)_2CHCOCl \rightarrow (C_2H_5)_2CHCONH_2$

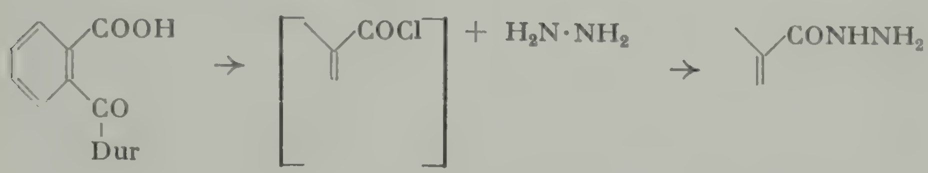
A soln. of α-ethylbutyryl chloride in dry benzene added dropwise during 1 hr. to benzene heated on a water bath while a stream of NH_3 is passed through and continued for 20 min. after the addition → α-ethylbutyramide. Y: 91%.—If NH_3 is passed directly into the soln. of the acid chloride, large quantities of diamides are formed. F. e. s. G. E. Philbrook, J. Org. Chem. *19*, 623 (1954).

Subst. carboxylic acid amides from carboxylic acid chlorides COCl → CON<

s. *9*, 474

Carboxylic acid hydrazides from carboxylic acids via carboxylic acid chlorides COCl → $CONHNH_2$

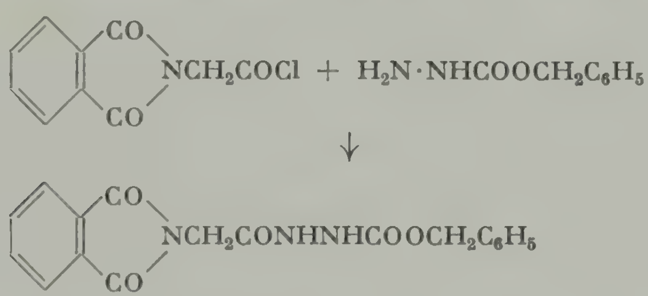
03.



A soln. of o-duroylbenzoic acid and $SOCl_2$ refluxed 1 hr., excess $SOCl_2$ distilled off, and the resulting acid chloride allowed to stand 24 hrs. with 85%-hydrazine hydrate at room temp. → o-duroylbenzoylhydrazine. Y: 90%. R. C. Fuson and W. C. Hammann, Am. Soc. *74*, 1626 (1952).

Carboxylic acid carbobenzoxyhydrazides COCl → CONHNHCOOR

04.



A soln. of phthalylglycyl chloride in ethyl acetate added to an ice-cold soln. of carbobenzoxyhydrazine in the same solvent, and the mixture kept 6 hrs. at room temp. → phthalylglycine carbobenzoxyhydrazide. Y: 89%. F. e. s. K. Hofmann et al., Am. Soc. *74*, 470, 476 (1952).

Isothiocyanates from amines NH_2 → N:C:S

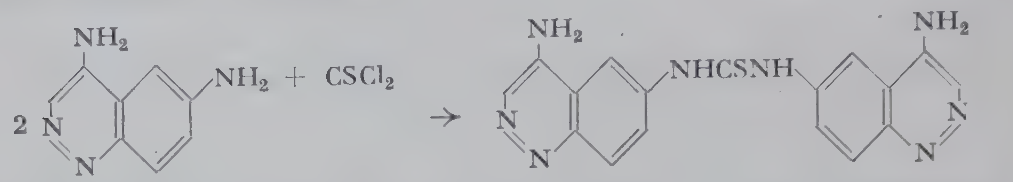
s. *1*, 464; s. a. Chem. and Ind. *1954*, 934

S-Thiocarbamic acid esters from amines and phenylthiocarbonyl chloride NH_2 → NHCOSR

s. *9*, 536

Sym. thioureas from amines $2\ RNH_2 \rightarrow (RNH)_2CS$

505.



A soln. of 10 g. 4,6-diaminocinnoline in 50% aq. acetone refluxed 0.5 hr. with thiocarbonyl dichloride → 13 g. N,N′-di-(4-amino-6-cinnolyl)-thiourea dihydrochloride. F. e. s. J. S. Morley and J. C. E. Simpson, Soc. *1952*, 2617.

Lithium *Li*

Tert. from prim. amines $NH_2 \rightarrow NR_2$

s. *3*, 366; s. a. J. Org. Chem. *19*, 1074 (1954)

Sodium hydroxide *NaOH*

Acylation of aminocarboxylic acids $NH \rightarrow NAc$

s. *9*, 501

Selective N-acylation of aminohydroxycarboxylic acids

506.

$$C_6H_5\overset{OH}{C}H\underset{NH_2}{C}HCOOH \rightarrow C_6H_5\overset{OH}{C}H\underset{NHCOC_6H_5}{C}HCOOH$$

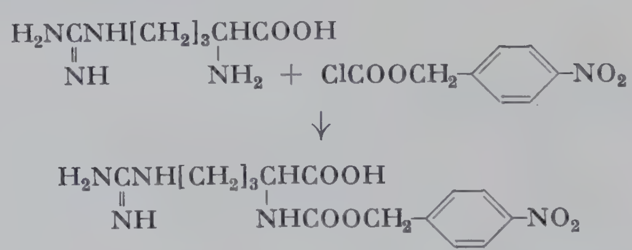
An aq. soln. of β-phenylserine and NaOH, and a soln. of benzoyl chloride in benzene stirred together while aq. NaOH is added slowly → N-benzoyl-β-phenylserine. Y: 80%. E. D. Bergmann, H. Bendas, and W. Taub, Soc. *1951*, 2673.

Carbalkoxy derivatives of amines $NH \rightarrow NCOOR$

s. *7*, 366, 490; carbo-p-nitrobenzoxy derivatives s. D. T. Gish and F. H. Carpenter, Am. Soc. *75*, 950 (1953)

Selective N-carbalkoxylation

507.



A soln. of p-nitrobenzyl chloroformate in dioxane and 4 *N* NaOH added portionwise during ca. 1 hr. to a soln. of L-arginine monohydrochloride

in aq. NaOH-NaHCO$_3$ of pH 10.0 → N$^\alpha$-p-nitrobenzoxycarbonyl-L-arginine. Y: 88%.—The guanido group is blocked with a proton. N$^\omega$-Isomer s. 49. D. T. Gish and F. H. Carpenter. Am. Soc. *75*, 5872 (1953); selective N-carbalkoxylation of aminohydroxycarboxylic acids s. J. A. Moore et al., Am. Soc. *76*, 2884 (1954).

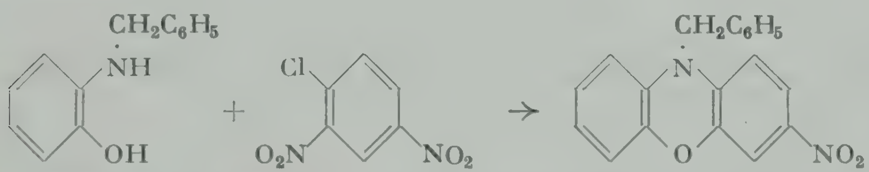
Carbalkoxycyanamides

508. $$C_2H_5OCOCl + H_2N\cdot CN \rightarrow C_2H_5OCONHCN$$

Ethyl chloroformate gradually added with stirring below 20° to cyanamide and NaOH in water, stirring continued 30 min., chloroform added, cooled, and acidified with concd. HCl → carbethoxycyanamide. Y: 88.5%. F. e., and decomposition products. s. D. W. Kaiser and J. T. Thurston, J. Org. Chem. *17*, 185 (1952).

Phenoxazines ○

509.



A soln. of NaOH in 50% aq. alcohol slowly added to a stirred refluxing soln. of 8.5 g. o-benzylaminophenol (prepn. s. 80) and 9 g. 1-chloro-2,4-dinitrobenzene in alcohol, heating continued for 1 hr. → 11.3 g. 10-benzyl-3-nitrophenoxazine. F. e. s. B. Boothroyd and E. R. Clark, Soc. *1953*, 1499.

Potassium hydroxide *KOH*

Betaines from aminocarboxylic acids ←

510. $$\underset{NH_2}{\underset{|}{CH_2}}CH(OH)CH_2COOH + 3\,CH_3I \rightarrow \underset{\overset{+}{N}(CH_3)_3}{\underset{|}{CH_2}}CH(OH)CH_2COO^-$$

A soln. of methyl iodide in methanol added to an aq. soln. of β-hydroxy-γ-aminobutyric acid and KOH, refluxed slowly for 36 hrs., at a pH of ca. 5.5, and the product purified by extraction with phenol satd. with water from an aq. soln. → DL-carnitine. Y: 78%. H. E. Carter and P. K. Bhattacharyya, Am. Soc. *75*, 2503 (1953).

Acyldicyanodiamides NH → NAc

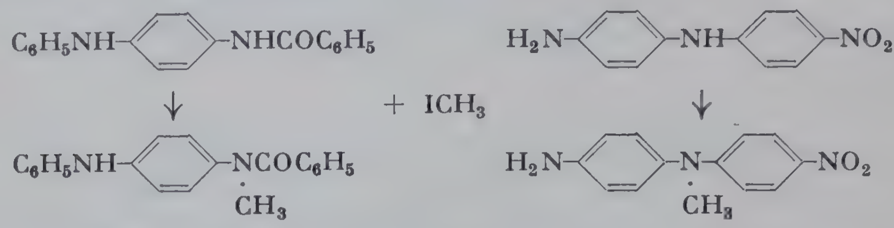
511. $$C_6H_5COCl + H_2N\underset{NH_2}{C}{=}NC{\equiv}N \rightarrow C_6H_5CONH\underset{NH_2}{C}{=}NC{\equiv}N$$

A mixture of dicyanodiamide, 85%-KOH pellets, and acetone stirred vigorously at 10° for 1 hr., then benzoyl chloride added with stirring at 0-5° → benzoyldicyanodiamide (startg. m. f. 219, 417). Crude Y: 89%. F. e., also with carboxylic acid anhydrides, s. P. Adams et al., J. Org. Chem. *17*, 1162 (1952).

Potassium hydroxide/acetone

Selective N-alkylation NH → NR
Substitution of carboxylic acid amides

512.

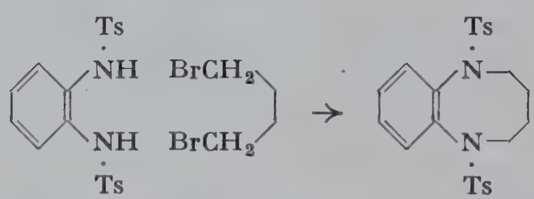


Powdered KOH added to p-benzamidodiphenylamine in acetone, the hot mixture refluxed gently while methyl iodide in acetone is added, and the product isolated after 20 min. → p-(N-methylbenzamido)diphenylamine. Y: 90%.—When large differences in proton availability exist, the method may also be applied to the selective methylation of one amino group in the presence of another: p-Amino-p′-nitrodiphenylamine → p-amino-p′-nitrodiphenylmethylamine. Y: 83%. F. e. s. I. J. Pachter and M. C. Kloetzel, Am. Soc. *74*, 1321 (1952).

Sodium/alcohol *NaOR*

Ring closure due to steric hindrance ○

513.

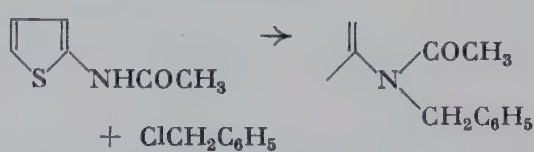


N,N′-Ditosyl-o-phenylenediamine added to a refluxing soln. of Na in n-butanol, refluxed until dissolved, 1,4-dibromobutane added, and refluxing continued until alkaline reaction disappears → N,N′-ditosyl-N,N′-tetramethylene-o-phenylenediamine. Y: 91%.—Polycondensation is inhibited by steric hindrance. It is therefore not necessary to apply high dilution (cf. 971). F. e. and limitations s. H. Stetter, B. *86*, 197 (1953); *dimethylformamide* as solvent s. B. *87*, 566 (1954).

Lithium amide *$LiNH_2$*

N-Alkylation NH → NR
Substitution of carboxylic acid amides

514.



A mixture of 2-acetamidothiophene, benzyl chloride, and $LiNH_2$ in dry toluene refluxed 24 hrs. → N-benzyl-N-(2-thienyl)acetamide. Y: 84%. I. A. Kaye, C. L. Parris, and N. Weiner, Am. Soc. *75*, 744 (1953); N-alkylation of 2-aminothiazoles s. Am. Soc. *74*, 2921 (1952).

Sodium amide *$NaNH_2$*

α,β-Acetylene-prim-amines from α,β-acetylenechlorides $Cl \rightarrow NH_2$

15. $$n\text{-}C_5H_{11}\cdot\overset{\overset{\displaystyle Cl}{\cdot}}{\underset{\underset{\displaystyle CH_3}{\cdot}}{C}}\cdot C{\equiv}CH \rightarrow n\text{-}C_5H_{11}\overset{\overset{\displaystyle NH_2}{\cdot}}{\underset{\underset{\displaystyle CH_3}{\cdot}}{C}}\cdot C{\equiv}CH$$

Methyl-n-amylethynylcarbinyl chloride in anhydrous ether added dropwise during 1 hr. with stirring to $NaNH_2$ in liq. NH_3, and stirring continued for 1 hr. → methyl-n-amylethynylcarbinyl amine. Y: 48-70%. F. e. and limitation s. G. F. Hennion and E. G. Teach, Am. Soc. *75*, 1653 (1953).

N-Alkylation $NH \rightarrow NR$

s. *9*, 539; s. a. U. Hörlein, B. *87*, 463 (1954)

m-Amines from o-halides with rearrangement ←

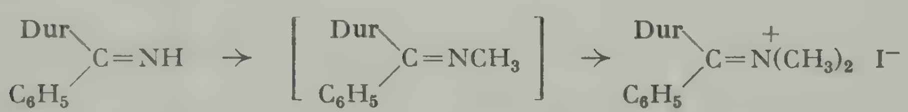
s. *3*, 371; s. a. J. F. Nobis and N. W. Burske, Am. Soc. *76*, 3034 (1954); also without rearrangement s. R. A. Benkeser and W. E. Buting, Am. Soc. *74*, 3011 (1952)

Potassium amide *KNH_2*

s. *9*, 539

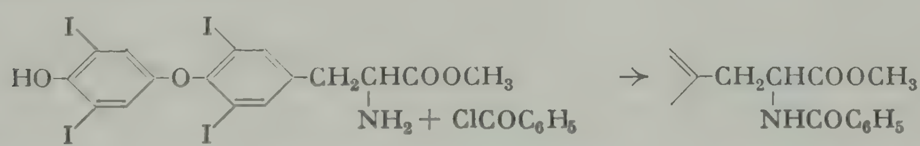
Sodium carbonate *Na_2CO_3*

Ketimine methiodides ←

16. 

A mixture of 5 g. duryl phenyl ketimine, 20 ml. 5%-Na-carbonate soln., and 10 g. methyl iodide refluxed 2 hrs. → duryl phenyl N-methylketimine methiodide. Y: 80%. F. e. s. R. C. Fuson, W. D. Emmons, and J. P. Freeman, Am. Soc. *75*, 5321 (1953).

Selective N-acylation $NH \rightarrow NAc$

17. 

2 *N* Na_2CO_3 then in portions benzoyl chloride in chloroform added with shaking to a soln. of L-thyroxine methyl ester in chloroform → N-benzoyl-L-thyroxine methyl ester. Y: 82%. F. e. s. A. Taurog, S. Abraham, and I. L. Chaikoff, Am. Soc. *75*, 3473 (1953).

Cyclic imines from dihalides ○

s. *2*, 438; from dichlorides s. B. Idson and D. E. Spoerri, Am. Soc. *76*, 2902 (1954)

Sodium hydrogen carbonate *$NaHCO_3$*

1,3,5-Triazine derivatives

518. A hot soln. of cyanuric chloride in acetone or dioxane poured in fine stream into water cooled to 0° at such a rate that the temp. does not exceed 5°, to the slurry thus formed 2-aminothiazole added, then excess aq. $NaHCO_3$ added gradually with stirring, which is continued 0.5-3 hrs. at 0-5° → 2,4-dichloro-6-(2-thiazolylamino)-1,3,5-triazine. Y: 70%.—Diamino derivatives demand a reaction temp. of 40-45°, triamino derivatives 100-125°. F. e. s. W. O. Foye and A. E. Buckpitt, J. Am. Pharm. Assoc. *41*, 385 (1952).

Sec. from prim. amines and fluorides

s. *8*, 563; 2,4-dinitrophenyl-L-amino acids s. K. R. Rao and H. A. Sober, Am. Soc. *76*, 1328 (1954)

Subst. hydrazines

s. *9*, 988

Potassium carbonate *K_2CO_3*

Urethans from amines $NH_2 \rightarrow NHCOOR$

519. $(C_6H_5CH_2OOC)_2CHNH_2 + ClCOOCH_2C_6H_5 \rightarrow (C_6H_5CH_2OOC)_2CHNHCOOCH_2C_6H_5$

A soln. of benzyl chloroformate in toluene added dropwise over a period of 3 hrs. to a stirred refluxing soln. of dibenzyl aminomalonate in dry benzene containing anhydrous K-carbonate, and refluxing continued 1 hr. → dibenzyl carbobenzoxyaminomalonate. Y: 86% based on benzyl chloroformate. H. M. Kissman and B. Witkop, Am. Soc. *75*, 1967 (1953).

Sodium azide *NaN_3*

Azides from halides $Hal \rightarrow N_3$

s. *7*, 493; s. a. F. R. Benson, L. W. Hartzel, and E. A. Otten, Am. Soc. *76*, 1858 (1954)

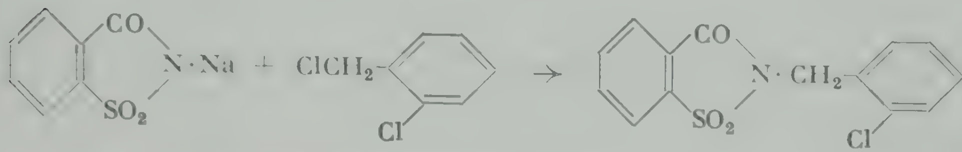
α-Azidoketones

s. *9*, 485; s. a. H. Bretschneider and H. Hörmann, M. *84*, 1021 (1953)

Sodium salt *Na⁺*

N-Alkylation of 2,4-oxazolidinediones NH → NR

s. *9*, 24

20. 

of sulfimides. Na-Saccharin and NaI added to a soln. of o-chlorobenzyl chloride in dimethylformamide, and heated 30 min. on a steam bath → N-(o-chlorobenzyl)saccharin. Y: 94%.—The less reactive normal and branched chained alkyl chlorides give best yields when the reaction is carried out at 150°. F. e. s. H. L. Rice and G. R. Pettit, Am. Soc. *76*, 302 (1954).

(Diacylamino)carboxylic acid esters from acylaminocarboxylic acid esters via (carbalkoxyalkylimino)chlorides ←

21. $$C_6H_5CH_2OOC\cdot CH_2NHCOC_6H_5 \rightarrow C_6H_5CH_2OOC\cdot CH_2N{=}\underset{\displaystyle Cl}{\underset{|}{C}}\cdot C_6H_5 + NaOOC\cdot C_6H_5 \rightarrow C_6H_5CH_2OOC\cdot CH_2N(COC_6H_5)_2$$

PCl_5 added to a soln. of benzyl hippurate in dry dioxane, swirled 10 min. until the PCl_5 is dissolved, then evaporated below 50°/25 mm. toluene added. and again evaporated at 25 mm pressure to remove the last traces of $POCl_3$, the crude imino chloride dissolved in dry dioxane. added to a stirred suspension of dry Na-benzoate in dioxane, warmed 12 hrs. at 65° with stirring, finally refluxed 4 hrs. → N,N-dibenzoylglycine benzyl ester. Y: 70%. J. C. Sheehan and E. J. Corey, Am. Soc. *74*, 4555 (1952).

Isothiocyanates from halides Hal → NCS

22. 

3-Bromocyclohexene added dropwise with stirring over a period of 2 hrs. to a soln. of Na-thiocyanate in abs. methanol, stirring continued at room temp. for an additional 2 hrs., and worked up with final vacuum distillation → 3-isothiocyanocyclohexene. Y: 76%. F. L. Greenwood and W. J. James. Am. Soc. *73*, 4495 (1951); cf. Synth. Meth. *8*, 411, 682.

Pyridine *C_5H_5N*

Tritylamines NH → NR

523. $$(C_6H_5)_3C \cdot Cl + H_2NC_6H_5 \rightarrow (C_6H_5)_3C \cdot NHC_6H_5$$

A soln. of trityl chloride in pyridine added to a soln. of aniline in pyridine, cooled to keep the mixture at room temp., and the product isolated after 24 hrs. → N-tritylaniline. Y: 88%. F. e. s. P. E. Verkade et al., R. *71*, 1007 (1952).

Tert. from. sec. amines
via carboxylic acid amides

524. $$(C_6H_5)_2CH\overset{CH_3}{\dot{N}}H + ClCOC_{10}H_7\text{–}\alpha \rightarrow (C_6H_5)_2CH\overset{CH_3}{\dot{N}}COC_{10}H_7\text{–}\alpha$$
$$\downarrow$$
$$(C_6H_5)_2CH\overset{CH_3}{\dot{N}}CH_2C_{10}H_7\text{–}\alpha$$

N-Methylbenzhydrylamine and α-naphthoyl chloride in dry pyridine heated 12 hrs. at 100°, then allowed to stand overnight → N-α-naphthoyl-N-methylbenzhydrylamine (Y: 97%) refluxed 2.5 hrs. with $LiAlH_4$ in ether, then stirred 12 hrs. at 20°, and the product isolated as the hydrochloride → N-methyl-N-α-methylnaphthylbenzhydrylamine hydrochloride (Y: 83%). F. e. and methods s. H. Dahn, U. Solms, and P. Zoller, Helv. *35*, 2117 (1952).

Sec. and tert. acid amides ←
Nitriles from carboxylic acid amides

525. $$2\ m\text{–}BrC_6H_4COCl + H_2NCOCH_3 \rightarrow (m\text{–}BrC_6H_4CO)_2NCOCH_3$$

Pyridine followed by acetamide added with stirring at −75° to a soln. of m-bromobenzoyl chloride in chloroform-methylene chloride, then ethanol added, and the mixture allowed to come to room temp. → di-(m-bromobenzoyl)acetamide. Y: 93%.—In certain cases, dehydration to nitriles occurs instead of acylation. F. e., also acylation of sulfonamides, s. Q. E. Thompson, Am. Soc. *73*, 5841 (1951).

Halogenourethans from amines ←

s. *9*, 45

Copper *Cu*

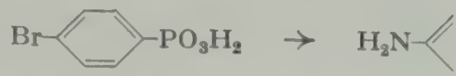
Oxindoles ○

s. *9*, 527

Cupric oxide *Cu_2O*

Replacement of bromine by amino groups ←
Sec. from prim. amines and halides

26.

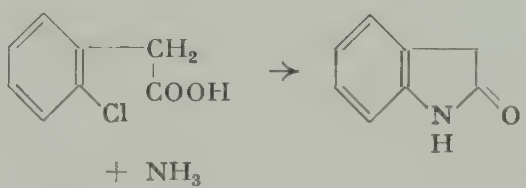


p-Bromobenzenephosphonic acid (prepn. s. 717) heated 6 hrs. in the presence of fresh Cu_2O in concd. aq. NH_3 at 100° → phosphanilic acid. Y: 80%. V. L. Bell, Jr., and G. M. Kosolapoff, Am. Soc. *75*, 4901 (1953); sec. from prim. amines s. G. O. Doak and L. D. Freedman, Am. Soc. *75*, 683 (1953).

Cupric acetate *$(CH_3COO)_2Cu$*

Oxindoles ○

27.



A mixture of o-chlorophenylacetic acid, Cu-powder or cupric acetate, and concd. aq. NH_3 heated 8 hrs. at 155-165° in a sealed tube → oxindole. Y: 34-43%. A. B. Neill, Am. Soc. *75*, 1508 (1953).

Silver nitrite *$AgNO_2$*

Aliphatic nitro compounds from halides Hal → NO_2
Victor Meyer reaction
Improved procedure

28. $n\text{-}C_5H_{11}Br \rightarrow n\text{-}C_5H_{11}NO_2$

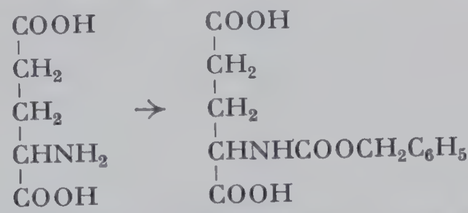
5% excess Ag-nitrite added with stirring as rapidly as possible at 3° to n-amyl bromide in petroleum ether (b. p. 45-55°), the ice bath removed, the temp. of the well-stirred mixture allowed to rise to 40° during 0.5 hr. and kept 5.5 hrs. at 38-42° by external cooling → 1-nitropentane. Y: 66.6%. F. e. s. C. W. Plummer and N. L. Drake, Am. Soc. *76*, 2720 (1954); in ether at lower temp. s. N. Kornblum, B. Taub, and H. E. Ungnade, Am. Soc. *76*, 3209 (1954); α,ω-dinitro compounds s. H. Feuer and G. Leston, Org. Synth. *34*, 37 (1954).

Magnesium oxide *MgO*

Subst. carboxylic acid amides COCl → CON<
from carboxylic acid chlorides

s. *9*, 402

Carbobenzoxylation of amines $NH_2 \rightarrow NHCOOR$

529. 

Carbobenzoxy chloride added portionwise during 30 min. with stirring to a mixture of glutamic acid, MgO, water, and ether, stirring continued for 6 hrs. → carbobenzoxy-L-glutamic acid. Y: 80%. V. du Vigneaud and G. L. Miller, Biochem. Prep. *2*, 79 (1952); s. a. Am. Soc. *76*, 6202 (1954).

Alkylmagnesium halide *RMgHal*

N-Acylation $NH \rightarrow NAc$

s. *7*, 494; 1-acylindoles s. G. R. Clemo and J. C. Seaton, Soc. *1954*, 2582; 10-acylphenothiazines s. G. Cauquil and A. Casadevall, C. r. *236*, 1569 (1953)

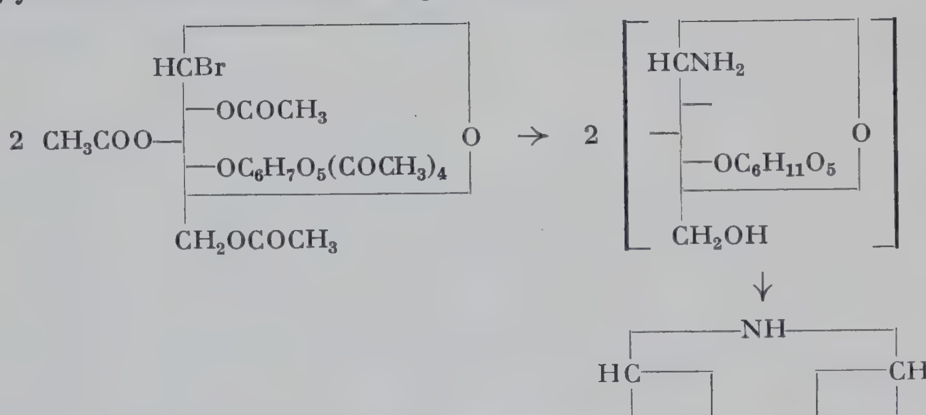
Mercuric chloride *$HgCl_2$*

Nucleosides from purines via mercuripurines ←

s. *7*, 497; improved procedure by addition of Celite in the second step s. B. R. Baker et al., J. Org. Chem. *19*, 1780, 1786 (1954)

Ethyl alcohol *C_2H_5OH*

Diglycosamines from acetohalogenosugars ←

530. 

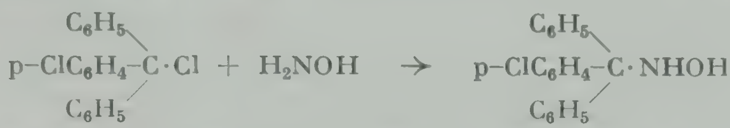
Finely powdered acetobromocellobiose added with shaking to liq. NH_3, which is then allowed to evaporate slowly, several times extracted with abs. methanol and evaporated to dryness in vacuo, again dissolved in abs. methanol, precipitated with abs. ether, and recrystallized several times with methanol-NH_3 → dicellobiosylimine. Y: 70%. Also isolation of the intermediate glycosamine s. F. Micheel et al., B. 85, 1092 (1952).

Phenol/hydrochloric acid *C_6H_5OH/HCl*

s. Hydrochloric acid/phenol

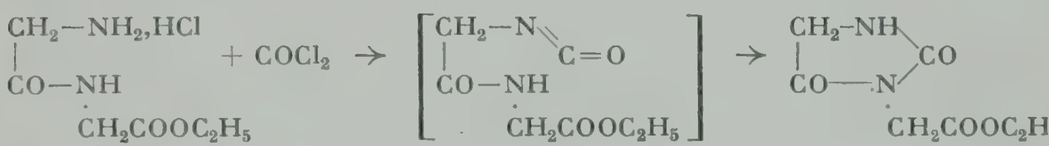
Hydrochloride ←

Hydroxylamines from halides Hal → NHOH

31. 

A soln. of 0.139 mole Na in abs. alcohol added to a warm soln. of 0.147 mole hydroxylamine hydrochloride in abs. alcohol, cooled to 0°, an ethereal soln. of p-chlorophenyldiphenylcarbinyl chloride added, and worked up after 1 hr. → p-chlorophenyldiphenylmethylhydroxylamine. Y: 78%. F. e. s. M. S. Newman and P. M. Hay, Am. Soc. 75, 2322 (1953).

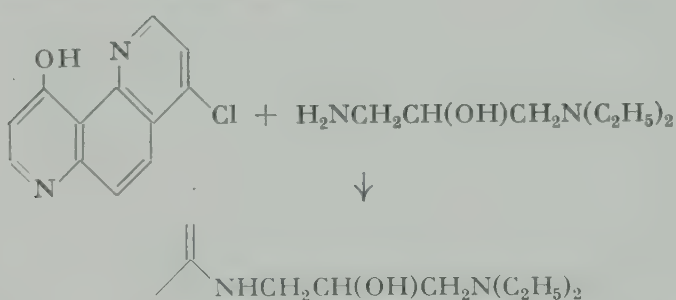
Hydantoins from phosgene ○

32. 

A suspension of glycylglycine ethyl ester hydrochloride in toluene treated with phosgene at an oil bath temp. of 130-160° for 3 hrs. until dissolved → ethyl 3-hydantoinacetate. Y: ca. 100%. S. Goldschmidt and M. Wick, A. 575, 217 (1952).

Hydrochloric acid/phenol *HCl/C_6H_5OH*

Sec. from prim. amines and halides NH_2 → NHR

33. 

A mixture of 4-chloro-10-hydroxy-1,7-phenanthroline, 3-diethylamino-2-hydroxypropylamine (prepn. s. 634), phenol, and alc. HCl in isopropanol refluxed 3 hrs. with stirring → 4-(3-diethylamino-2-hydroxypropylamino)-10-hydroxy-1,7-phenanthroline. Y: 87%. F. e. s. A. R. Surrey and R. A. Cutler, Am. Soc. 76, 1109 (1954); role of phenol s. a. A. P. Phillipps, J. Org. Chem. 17, 1456 (1952).

Sulfur ↑

NC⇅S

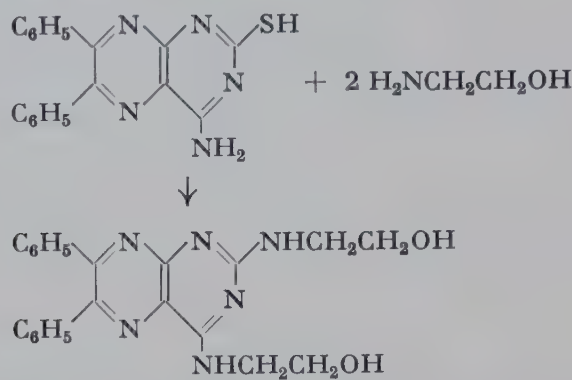
Without additional reagents *w.a.r.*

Replacement of sulfur by amino groups ←

s. *9*, 542

Exchange of substituents
of pyrimido[4,5-b]pyrazines
Replacement of sulfhydryl by amino groups
Sec. from prim. amines ←

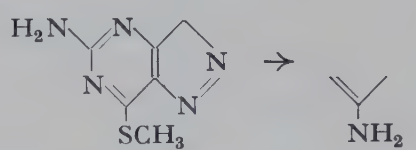
534.



A mixture of 4-amino-2-mercapto-6,7-diphenylpteridine and ethanolamine refluxed 4 hrs. → 2,4-bis-(2-hydroxyethylamino)-6,7-diphenylpteridine. Y: ca. 100%. F. e. s. E. C. Taylor, Jr., and C. K. Cain, Am. Soc. *73*, 4384 (1951).

Amines from thioethers $SR \rightarrow NH_2$

535.



5 g. 5-amino-7-methylthio-1,2,4,6-tetraazaindene and aq. NH_3 (d. 0.88) heated 16 hrs. at 150° in a sealed tube → 2.8 g. 5,7-diamino-1,2,4,6-tetraazaindene. F. L. Rose, Soc. *1952*, 3448; tert. amines s. C. K. Cain and S. K. Naegele, Am. Soc. *76*, 3214 (1954).

Ureas and semicarbazides
from thiocarbonyl chlorides
via S-thiocarbamic acid esters ←

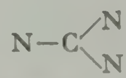
536. $C_2H_5NH_2 + ClCOSC_6H_5 \rightarrow C_2H_5NHCOSC_6H_5 + H_2NC_2H_5$

$$\downarrow$$

$$C_2N_5NHCONHC_2H_5$$

Ethylamine added portionwise over a 3-4 min. interval to an ice-cold and vigorously shaken soln. of phenylthiocarbonyl chloride in abs.

alcohol, and allowed to stand 10 min. at 25° → N-ethyl-S-phenylthiocarbamate (Y: 84%) dissolved in abs. ethanol, ethylamine added to the ice-cold soln. with shaking, and allowed to stand 15 min. at 25° → crude sym-diethylurea (Y: 90%). Also one-step procedure, asym. ureas, and use of triethylamine in the second step, s. W. H. Schuller and C. Niemann, Am. Soc. *75*, 3425 (1953); also acylureas and semicarbazides from S-thiocarbamic acid esters and amides or hydrazines respectively s. D. G. Crosby and C. Niemann, Am. Soc. *76*, 4458 (1954).

Guanidines from amines and isothioureas 

s. *2*, 456; *5*, 346; nitroguanidines s. L. Fishbein and J. A. Gallaghan, Am. Soc. *76*, 1877 (1954)

Thionocarbamic acid esters from thionothiodiformic acid esters ←

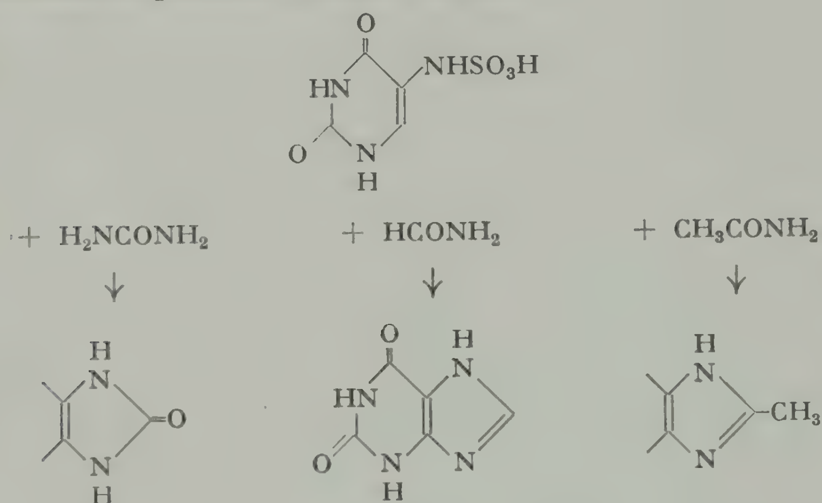
537.

$$C_6H_5NH_2 + S\begin{array}{l} \diagup COOC_2H_5 \\ \diagdown CSOC_2H_5 \end{array} \rightarrow C_6H_5NHCSOC_2H_5 + C_2H_5OH + COS$$

Aniline added dropwise with stirring to an alc. soln. of diethyl thionothiodiformate cooled in an ice-salt bath, and stirring continued for 3 hrs. → ethyl phenylthionocarbamate. Y: 87%. F. e. s. R. Sayre, Am. Soc. *74*, 3647 (1952).

New synthesis of purines from pyrimidines ○

538.



A mixture of 2-sulfaminouracil (prepn. s. 675) and

urea heated 30 min. at 190-200° → uric acid. Y: 90%.	formamide heated to 200°, and kept 40 min. at this temp. → xanthine. Y: 75-80%.	acetamide heated 30 min. at 200° → 8-methylxanthine. Y: 75 to 80%.

F. G. Fischer, W. P. Neumann, and J. Roch, B. *85*, 752 (1952).

Sodium hydroxide *NaOH*

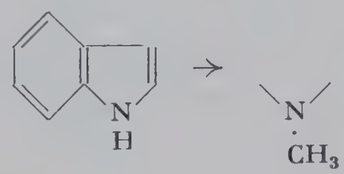
N-Alkylation of sulfonylamides NH → NR

s. *6*, 410; s. a. B. R. Baker, R. E. Schaub, and J. P. Joseph, J. Org. Chem. *19*, 638 (1954)

Sodium amide *$NaNH_2$*

N-Alkylation of indoles NH → NR

539.

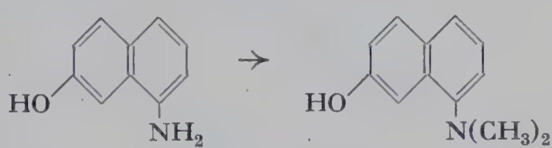


Indole added with stirring to a soln. of $NaNH_2$ in *liq. NH_3*, then dimethyl sulfate in abs. ether added dropwise during 30 min., and stirring continued for 1 hr. → N-methylindole. Y: 90%.—Other procedures give C-alkylated products. F. e. with halides s. H. Plieninger, B. *87*, 127 (1954); s. a. K. T. Potts and J. E. Saxton, Soc. *1954*, 2641; with KNH_2 in liq. NH_3 s. J. W. Cook, J. D. Loudon, and P. McCloskey, Soc. *1952*, 3904.

Sodium hydrogen carbonate *$NaHCO_3$*

Selective N-methylation of ar. amines

540.



Ar. amines are methylated in the presence of neutral carbonates ($NaHCO_3$, $KHCO_3$, $CaCO_3$) under conditions in which phenolic hydroxyl groups are not methylated.—E: A mixture of crude 1-amino-7-naphthol, $NaHCO_3$, dimethyl sulfate, water, and ethyl acetate stirred 3 hrs. at 20-23° until the gas evolution ceases, then excess dimethyl sulfate decomposed by treating with concd. aq. NH_3 and stirring 10 min. → 1-dimethylamino-7-naphthol. Y: 74%. F. e., also quaternary ammonium salts, s. S. Hünig, B. *85*, 1056 (1952).

Triethylamine *$(C_2H_5)_3N$*

Disubst. ureas from S-thiocarbamic acid esters ←

s. *9*, 536

Pyridine C_5H_5N

Carboxylic acid anilides from carboxylic acids and sulfamides
Formamidines from sulfamides ←

541. $$C_6H_5CH_2COOH + (C_6H_5NH)_2SO_2 \rightarrow C_6H_5CH_2CONHC_6H_5$$

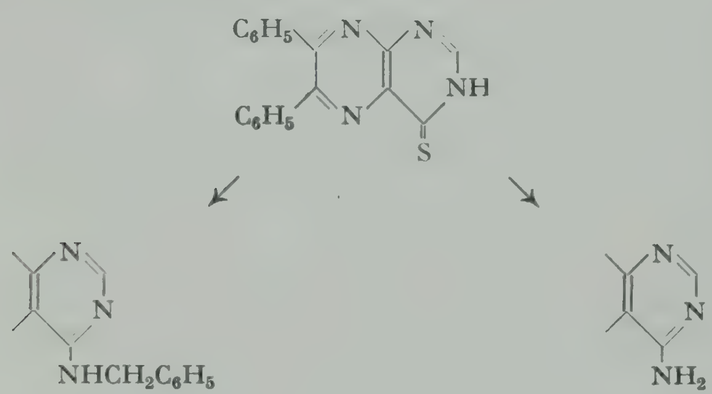
$$HCOOH + 2\,(C_6H_5NH)_2SO_2 \rightarrow HC\begin{cases} NC_6H_5 \\ NHC_6H_5 \end{cases}$$

A mixture of phenylacetic acid, sym. diphenylsulfamide, and dry pyridine heated 4 hrs. at 115-120° → α-phenylacetanilide. Y: 97.1%.—Formic acid reacts with 2 moles giving 87% diphenylformamidine. F. e. s. A. V. Kirsanov and N. L. Egorova, Ж. *22*, 1612, 1614 (1952); C. A. *47*, 8041b, a.

Mercuric oxide *HgO*

Replacement of sulfur by amino groups ←

542.



A mixture of 6,7-diphenyl-4(3H)-pteridinethione,

benzylamine, HgO, and ethanol refluxed 5 hrs. → 4-benzylamino-6,7-diphenylpteridine. Y: 99%.

and abs. ethanol satd. with NH_3 heated 10 hrs. at 130° in a sealed tube → 4-amino-6,7-diphenylpteridine. Y: 84%.—This compound could not be obtained under less strenuous conditions with HgO.

F. e. s. E. C. Taylor, Jr., J. A. Carbon, and D. R. Hoff, Am. Soc. *75*, 1904 (1953).

Sulfur *S*

Sym. thioureas from amines $CS(N\langle)_2$

s. *6*, 489; f. methods s. S. Hünig, H. Lehmann, and G. Grimmer, A. *579*, 77 (1953)

Hydriodides ←

Aminoguanidines from isothioureas SR → $NHNH_2$

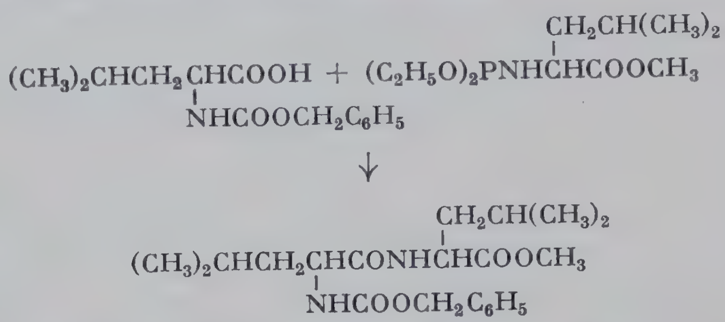
s. 8, 532; also cyclic compounds s. W. G. Finnegan, R. A. Henry, and E. Lieber, J. Org. Chem. *18*, 779 (1953)

Remaining Elements ↓ NC⇅ Rem

Without additional reagents *w.a.r.*

Synthesis of peptides with phosphite amides COOH → CONHR

543.

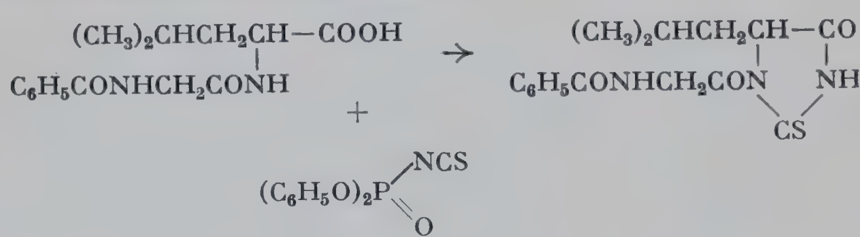


Methyl L-leucinate diethyl phosphite amide refluxed 1 hr. with carbobenzoxy-L-leucine in toluene → methyl carbobenzoxy-L-leucyl-L-leucinate. Y: 74%.—This new amide synthesis differs from the usual methods in that the intermediate is a reactive derivative of the amino moiety rather than the carboxylic fragment. Y: 74%. F. e. s. G. W. Anderson et al., Am. Soc. *74*, 5304 (1952).

Triethylamine $(C_2H_5)_3N$

Stepwise degradation of peptides via 2-thiohydantoins Modified Schlack-Kumpf degradation ○

544.



cf. Synth. Meth. 8, 475.
The following procedure gives high yields of the intermediate acylthiohydantoins under mild conditions: Triethylamine, then diphenyl isothiocyanophosphonate added to a soln. of benzoylglycylleucine in dimethylformamide, and kept 2 days at room temp. in a sealed flask → 1-benzoylglycyl-5-isobutyl-2-thiohydantoin. Y: over 90%. F.e., in acetonitrile, s. G. W. Kenner, H. G. Khorana, and R. J. Stedman, Soc. *1953*, 673.

Carbon ↑ NC⇅C

Without additional reagents *w.a.r.*

Thiosemicarbazones by interchange CO → C:N·NHCSNH$_2$

s. *9*, 432

Formylation of amines NH → NCHO

45.

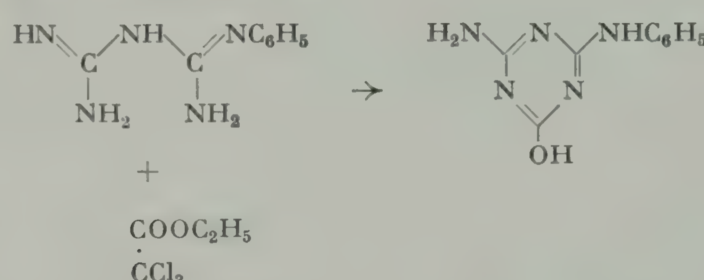
Strong organic bases can be easily formylated with chloral in good yield. A rapid reaction takes place at low temp., and chloroform is the only by-product.—E: 1 molar equivalent chloral added dropwise with stirring and ice-cooling to piperidine, stirred several hrs. at room temp., finally heated 0.5 hr. on a steam bath → N-formylpiperidine. Y: 90%.—Solid amines are dissolved or suspended in chloroform.—F. e. s. F. F. Blicke and Chi-Jung Lu, Am. Soc. *74*, 3933 (1952).

Carboxylic acid amides COOH → CONHR
from carboxylic acids and ureas

s. *2*, 461; also dicarboxylic acid imides s. A. Rahman and M. O. Farooq, B. *86*, 945 (1953)

1,3,5-Triazines from biguanides ○

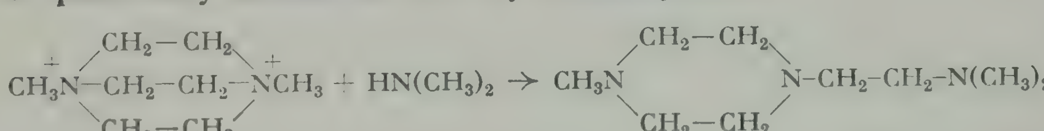
46.



Ethyl trichloroacetate added with stirring to a suspension of phenylbiguanide in chloroform, and refluxed 5 hrs. → 2-amino-4-anilino-6-hydroxy-1,3,5-triazine. Y: 83.6%. S. L. Shapiro and C. G. Overberger, Am. Soc. *76*, 97 (1954).

v. Braun degradation C
of quaternary ammonium salts by transalkylation

47.



Triethylendiamine di(methobromide) heated with dimethylamine and methanol in a sealed tube with shaking at 40° for 1 hr., then at 125° for 7 hrs., cooled and satd. with HCl → 1-(2-dimethylaminoethyl)-4-

methylpiperazine hydrochloride. Crude Y: 88%. F. e. s. O. Hromatka and O. Kraupp, M. *82*, 880 (1951).

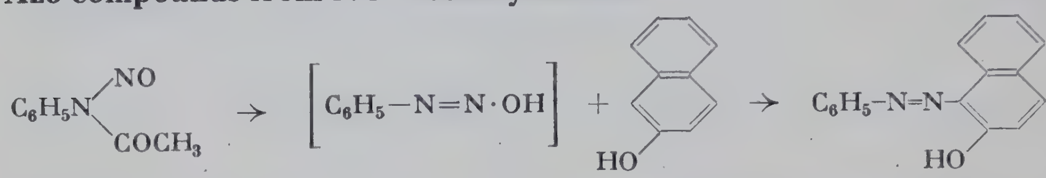
Sodium hydroxide *NaOH*

Japp-Klingemann reaction ←
Hydrazones from diazonium salts
α-Ketocarboxylic acid ester phenylhydrazones
from β-ketocarboxylic acid esters
s. *2*, 462, 813; s. a. V. V. Feofilaktov and N. K. Semenova, Sint. Org. *2*, 63 (1952); C. A. *48*, 666c

Sodium/alcohol *NaOR*

Azo compounds from N-nitrosoacylamines N:N

548.



An ice-cold alc. soln. of crude N-nitrosoacetanilide treated with β-naphthol, then with Na-ethoxide in ethanol, after 2 min. at 0° neutralized by dropwise addition of glacial acetic acid → phenylazo-2-naphthol. Y: 98.5%. R. Huisgen, A. *573*, 163 (1951).

Sodium amide *$NaNH_2$*

Carboxylic acid amides from phenyl ketones $COC_6H_5 \rightarrow CONH_2$
s. *2*, 463, 725; s. a. K. E. Hamlin and M. Freifelder, Am. Soc. *75*, 369 (1953)

Pyridine *C_5H_5N*

Subst. carboxylic acid amides from isocyanates N:C:O → NHCOR
Peptide synthesis via
α-isocyanatocarboxylic acid esters
s. *8*, 538; s. a. B. *86*, 1116 (1953)

Methylmagnesium iodide *CH_3MgI*

Replacement of N-acyl by N-alkyl NAc → NR

549.

$$C_6H_5N\begin{matrix} \diagup CH_2C_6H_5 \\ \diagdown COCH_3 \end{matrix} + ClCH_2CH_2N(CH_3)_2 \rightarrow C_6H_5N\begin{matrix} \diagup CH_2C_6H_5 \\ \diagdown CH_2CH_2N(CH_3)_2 \end{matrix}$$

N-Benzyl-N-phenylacetamide added in small portions to excess ethereal methyl-MgI, refluxed 1.5 hrs. with stirring, cooled in an ice bath, dimethylaminoethyl chloride hydrochloride added portionwise to the stirred mixture, and refluxed 2 additional hrs. → N,N-dimethyl-N′-benzyl-N′-phenylethylenediamine (Antergan). Y: 53.5%. Limitation s. I. A. Kaye, C. L. Parris, and N. Weiner, Am. Soc. *75*, 744 (1953).

Cyanogen bromide *CNBr*

Cyanamides from tert. amines NR → N·CN

s. 8, 540; s. a. A. Nickon and L. F. Fieser, Am. Soc. *74*, 5566 (1952)

Hydrazoic acid *HN_3*

Schmidt reaction $COOH \rightarrow NH_2$
Amines from carboxylic acids
Degradation with loss of 1 C-atom

s. 5, 354; in 100%-H_2SO_4 s. a. M. Fields, S. Rothchild, and M. A. Leaffer, Am. Soc. *74*, 2435 (1952)

Hydroxylamine/polyphosphoric acid *$H_2NOH/H(PO_3H)_xOH$*

Amines from carboxylic acids $COOH \rightarrow NH_2$
Lossen rearrangement

s. *8*, 542; s. a. Am. Soc. *76*, 3039 (1954)

Phosphorus oxychloride *$POCl_3$*

Exchange of substituents of amines NR → NR′

s. *9*, 625

Copper-chromium-barium oxide ←

Transalkylation of tert. amines

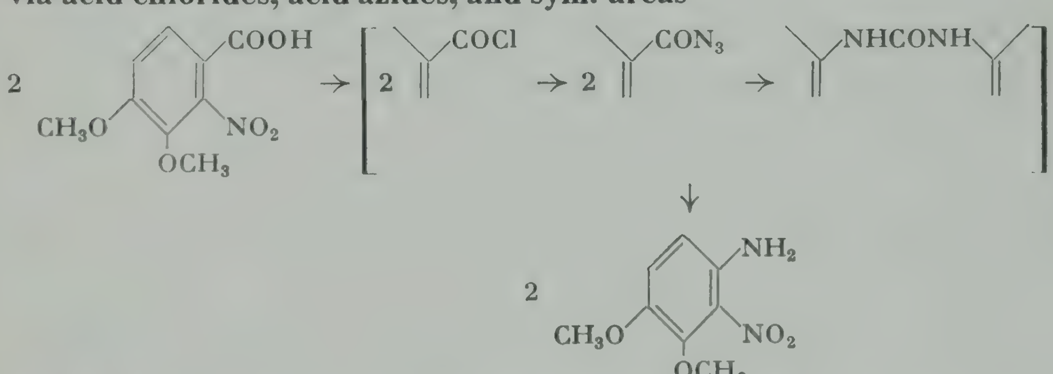
550. $$C_{11}H_{23}CH_2OH + N(C_2H_5)_3 \rightarrow C_{11}H_{23}CH_2N(C_2H_5)_2$$

A mixture of dodecanol, triethylamine, and Cu-Cr-Ba oxide heated 10 hrs. at 250° and 380 atm. of H_2 → diethyldodecylamine. Y: 66%. F. e. s. H. J. Schneider, H. Adkins, and S. M. McElvain, Am. Soc. *74*, 4287 (1952).

Via intermediates *v.i.*

Shortened Curtius degradation $COOH \rightarrow NH_2$
Amines from carboxylic acids
via acid chlorides, acid azides, and sym. ureas

551.



An aq. soln. of Na-azide added at 0-5° with stirring to a soln. of 2-nitroveratric acid chloride (prepared from the acid with $SOCl_2$), stir-

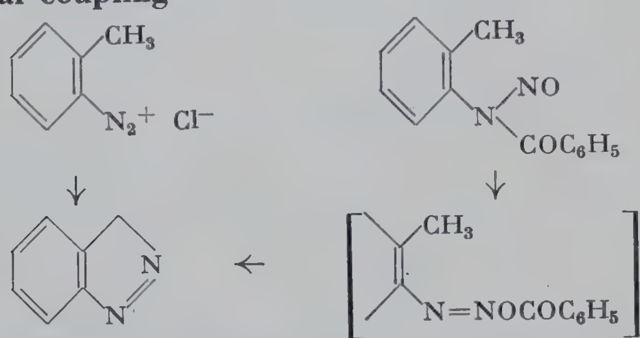
ring continued 0.5 hr. at 0°, poured into ice-water, the crude azide dried, dissolved in dry benzene, heated gently at first and then at reflux 4-6 hrs. until N_2-evolution ceases, cooled to room temp., vigorously stirred and treated cautiously with cold 50%-KOH soln., whereby the sym. urea precipitates, then the benzene slowly distilled from the reaction mixture, whereby the urea is hydrolyzed → 4-amino-3-nitroveratrole. Y: 85%. R. C. Elderfield and G. L. Krueger, J. Org. Chem. *17*, 358 (1952).

Elimination

Hydrogen ↑ NC ⇑ H

Tetramethylammonium acetate *$CH_3COON(CH_3)_4$*

Indazoles from diazonium salts or N-nitrosoacylamines. Intramolecular coupling ○

552. 

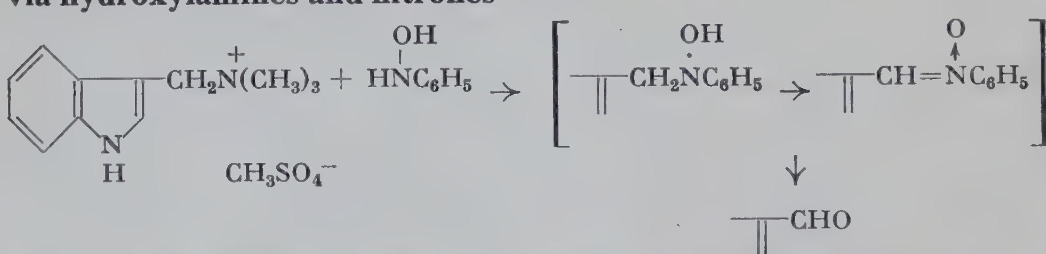
o-Toluenediazonium chloride added to a soln. of dry tetramethylammonium acetate in alcohol-free chloroform, and allowed to stand 1 day at room temp. → indazole. Y: 87%.

Crude nitrosobenz-o-toluidide in dry alcohol-free chloroform allowed to stand several days at room temp. → indazole. Y: 92%.

In alcohol, the yields of indazole are low, and ethyl alcohol is oxidized to acetaldehyde (Y: up to 81%). R. Huisgen and H. Nakaten, A. *573*, 181 (1951).

Nitrobenzene/sodium hydroxide *$C_6H_5NO_2/NaOH$*

Aldehydes from quaternary ammonium salts via hydroxylamines and nitrones $CH_2\overset{+}{N}R_3 \rightarrow CHO$

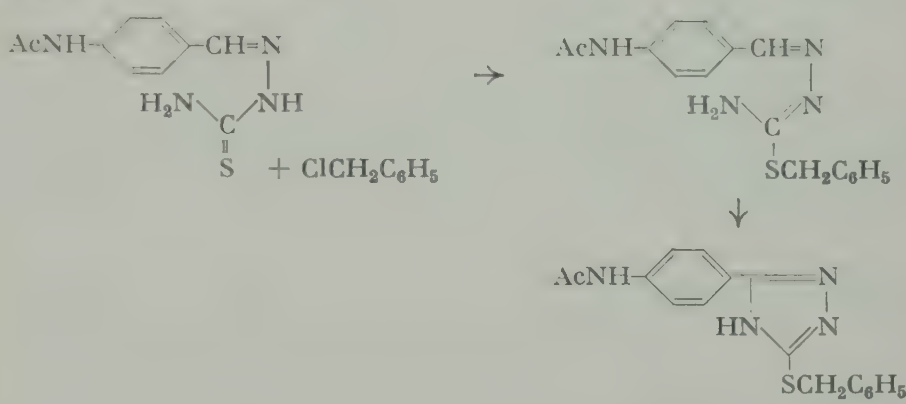
553. 

Phenylhydroxylamine added at room temp. to a soln. of gramine methosulfate in methanol, made alkaline with 2 *N* NaOH, nitrobenzene added,

refluxed 1 hr., more 2 *N* NaOH added, steam-distilled, and the product isolated from the residue → 3-indolealdehyde. Y: 87-91%. J. Thesing. B. *87*, 507 (1954).

Ferric chloride *$FeCl_3$*

3-Mercapto-1,2,4-triazoles from thiosemicarbazones via isothiosemicarbazones

554.


A mixture of 4-acetamidobenzaldehyde thiosemicarbazone and benzyl chloride refluxed 1.5 hrs. → 4-acetamidobenzaldehyde 3-benzyl-3-thiopseudosemicarbazone hydrochloride (Y: 73%), the crude compound dissolved in water, and to the boiling soln. aq. 10%-$FeCl_3$ added portionwise → 3-benzylmercapto-5-(4-acetamidophenyl)-1,2,4-triazole (Y: 73%). F. e. s. R. Duschinsky and H. Gainer, Am. Soc. *73*, 4464 (1951).

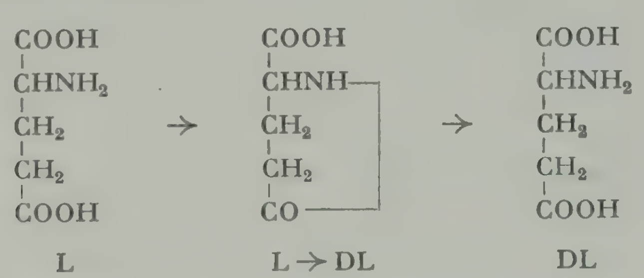
Oxygen ↑ NC ⇑ O

Without additional reagents *w.a.r.*

Lactam ring closure ○

s. *9*, 949

Racemization via lactams

555.


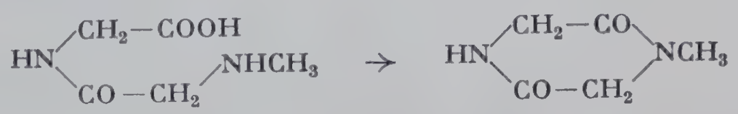
Mono-Na-L-glutamate and solid NH_4Cl thoroughly mixed, heated at 230-235° until evolution of NH_3 and water vapor ceases, heating continued 1 hr. with frequent stirring, refluxed 5 hrs. with 6 *N* HCl, and the aq. soln. of the crude product adjusted approximately to pH 3 with

concd. aq. NH_3 → DL-glutamic acid monohydrate. Y: 51-53%.—L-Pyrrolidone carboxylic acid racemizes rapidly at 230°. M. S. Dunn and M. P. Stoddard, Biochem. Prep. *2*, 69 (1952).

Indazoles from N-nitrosoacylamines

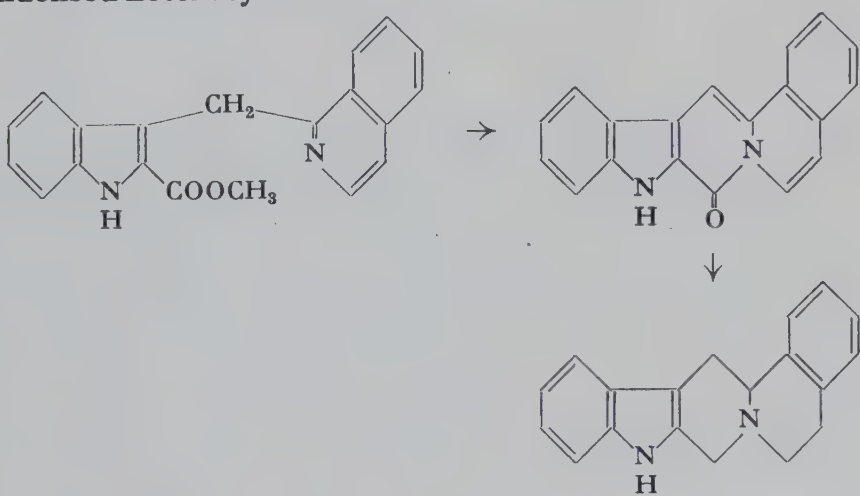
s. *9*, 552

2,5-Piperazinediones

556. 

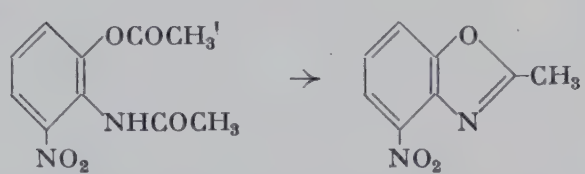
A mixture of sarcosylglycine and ethylene glycol refluxed 30 min. → 1-methyl-2,5-piperazinedione. Y: 73%. B. H. Chase and A. M. Downes. Soc. *1953*, 3874.

N-Condensed heterocyclics

557. 

A soln. of 1-(2′-carbomethoxyskatyl)isoquinoline in α-methylnaphthalene refluxed 20 hrs. → 1,2-benzo-7,8-(2′,3′-indolo)-6-quinolizone (Y: 85%), 1 g. suspended in boiling n-butanol, and Na added in small pieces → 0.9 g. 1,2-benzo-7,8-(2′,3′-indolo)tetrahydroquinolizine. V. Boekelheide and Chu-tsin Liu, Am. Soc. *74*, 4920 (1952); ring closure s. a. Am. Soc. *75*, 3679 (1953).

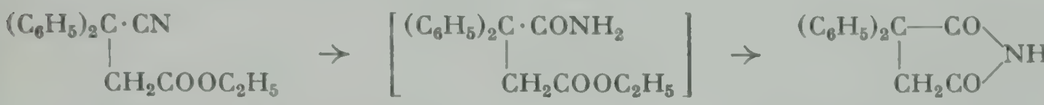
Benzoxazoles

558. 

3-Nitro-2-acetamido-1-phenyl acetate heated in an oil bath at 200° until fused, then at 230-240° until no more acetic acid distils → 2-methyl-4-nitrobenzoxazole. Y: 97%. C. Sannie and H. Lapin, Bl. *1952*, 369.

Sodium hydroxide *NaOH*

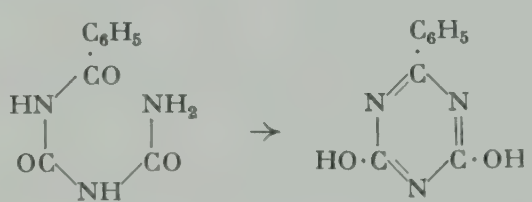
Dicarboxylic acid imides
from cyanocarboxylic acid esters
via dicarboxylic acid amide esters

9. 

Ethyl β-cyano-β,β-diphenylpropionate dissolved during 2-3 hrs. in cold 85%-H_2SO_4, the crude ester-amide dissolved in warm alcohol, aq. NaOH added, and immediately acidified with dil. HCl → α,α-diphenylsuccinimide. Y: ca. 100%. F. Salmon-Legagneur, Bl. *1952*, 580.

Potassium hydroxide *KOH*

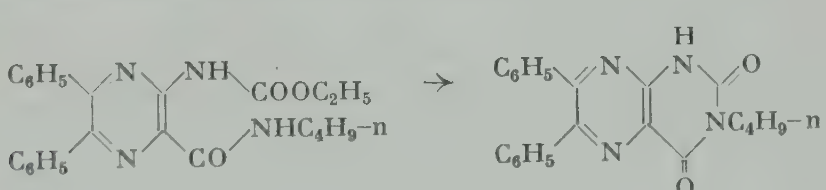
1,3,5-Triazines from acylbiurets

0. 

Benzoylbiuret (prepn. s. 219) dissolved in aq. KOH, and acidified 2 hrs. later → benzoguanamide. Crude Y: 98%. P. Adams et al., J. Org. Chem. *17*, 1162 (1952).

Sodium/alcohol *NaOR*

Pyrimido[4,5-b]pyrazines from pyrazines

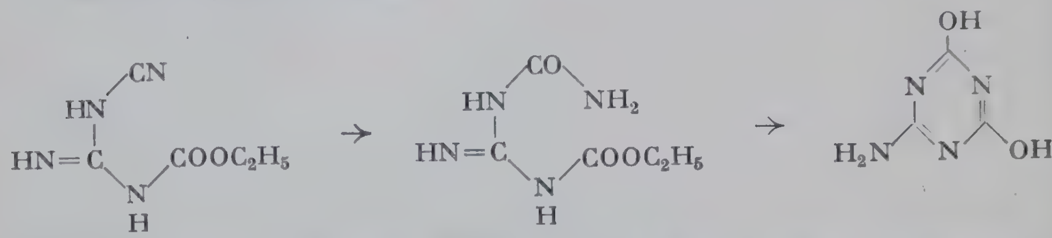
61. 

A soln. of N-(n-butyl)-3-carbethoxyamino-5,6-diphenylpyrazinamide in a soln. of Na in abs. ethanol refluxed 10 hrs. → 3-(n-butyl)-6,7-diphenyl-2,4(1H,3H)-pteridinedione. Y: 88.8%. F. methods s. E. C. Taylor, Jr., J. A. Carbon, and D. R. Hoff, Am. Soc. *75*, 1904 (1953); s. a. W. Pfleiderer and J. Geisler, B. *87*, 1274 (1954).

Ammonia *NH_3*

1,3,5-Triazines from carbalkoxydicyanodiamides via carbalkoxyguanylureas

562.



Carbethoxydicyanodiamide added to 18.5%-HCl, heating continued several min. after the exothermic reaction has subsided → carbethoxyguanylurea hydrochloride (Y: 85.5%) suspended in water and the equivalent amount of aq. NH_3 added → carbethoxyguanylurea. (Y: ca. 100%) heated with aq. NH_3 → ammelide (Y: 85%). D. W. Kaiser and J. T. Thurston, J. Org. Chem. *17*, 185 (1952).

Pyridine/carboxylic acid chloride *$C_5H_5N/RCOCl$*

s. Carboxylic acid chloride/pyridine

Alumina-silica *Al_2O_3-SiO_2*

Nitriles from carboxylic acid amides $CONH_2 \rightarrow CN$

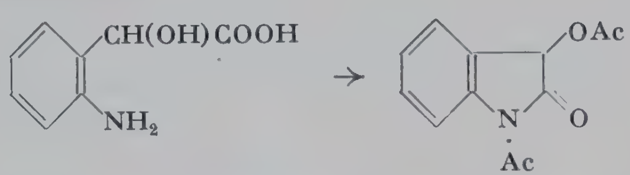
563. $(CH_3)_2CHCONH_2 \rightarrow (CH_3)_2CHC{\equiv}N$

Isobutyramide passed at 425° over alumina-silica gel → isobutyronitrile. Y: 90%. F. e. s. M. A. Naylor and A. W. Anderson, Am. Soc. *75*, 5392 (1953).

Acetic anhydride *$(CH_3CO)_2O$*

Dioxindole derivatives ○

564.



A suspension of 0.5 g. o-aminomandelic acid in acetic anhydride allowed to stand 2 days at room temp., then heated 0.5 hr. on a steam bath → 0.45 g. O,N-diacetyldioxindole. F. e. s. E. J. Alford and K. Schofield, Soc. *1952*, 2102.

Carboxylic acid chloride/pyridine *$RCOCl/C_5H_5N$*

Nitriles from carboxylic acid amides $CONH_2 \rightarrow CN$

s. *9*, 525

Phosphorus trichloride *PCl_3*

565. $(C_6H_5)_2CHCONH_2 \rightarrow (C_6H_5)_2CHCN$

Diphenylacetamide refluxed 2.5 hrs. with PCl_3 in benzene on a steam bath → diphenylacetonitrile. Y: 80%. F. Salmon-Legagneur, Bl. *1952*, 580.

Phosphorus pentachloride *PCl_5*

Lactam ring closure with simultaneous formation of carboxylic acid chlorides from carboxylic acids ○

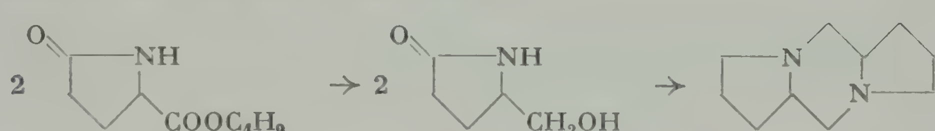
566.

PCl_5 added in one portion at 0° to a suspension of tosyl-L-glutamic acid in dry ether, and allowed to warm to room temp. toward the end of the reaction → 1-tosylpyroglutamyl chloride (startg. m. f. 402). Y: 90%. J. M. Swan and V. du Vigneaud, Am. Soc. *76*, 3110 (1954).

Copper chromite *$CuCr_2O_4$*

Decahydrodipyrrolo[a,d]pyrazines
Alcohols from carboxylic acid esters ○

567.

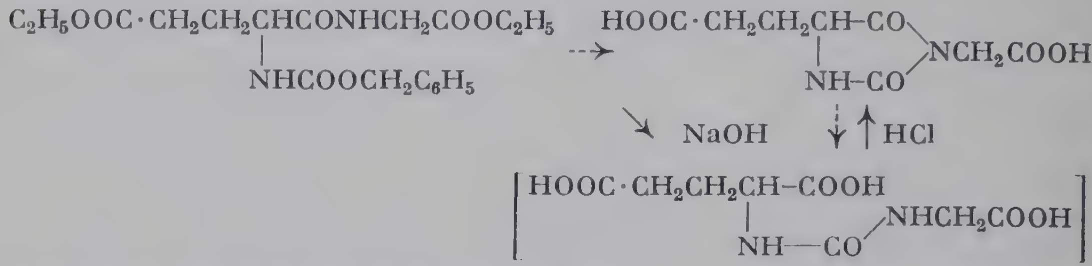


Butyl pyroglutamate hydrogenated 4 hrs. with $CuCr_2O_4$ in dioxane at 150°, the catalyst filtered off, the solvent completely removed by vacuum distillation, and the crude 5-hydroxymethyl-2-pyrrolidone (Y: 96% when isolated) hydrogenated 5.5 hrs. with $CuCr_2O_4$ in dioxane at 250° → decahydrodipyrrolo[a,d]pyrazine (Y from pure 5-hydroxymethyl-2-pyrrolidone almost 100%). Over-all Y: 77%.—Removal of the butanol formed in the first step prevents the formation of N-butyl-2-hydroxymethylpyrrolidine as by-product in the second step. E. Segel, Am. Soc. *74*, 851 (1952).

Hydrochloric acid *HCl*

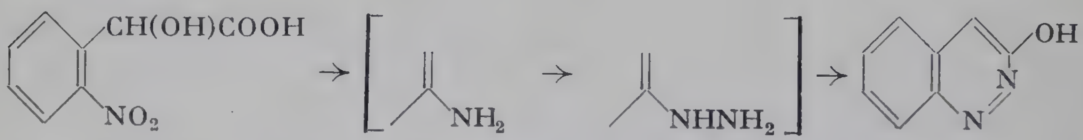
Hydantoins from α-ureidocarboxylic acids
s. *9*, 404

Hydantoins from N-carbalkoxypeptides via α-ureidocarboxylic acids
Differentiation between α- and γ-glutamylpeptides
Degradation of peptides via hydantoins

568. 

3 moles *N* NaOH added to a soln. of carbobenzoxy-α-D-glutamylglycine diethyl ester in ethanol, refluxed 2 hrs. on a water bath, acidified, evaporated to dryness, and the residue boiled 3 hrs. with concd. HCl → 5-(β-carboxyethyl)hydantoin-3-acetic acid. Y: 84%.—No hydantoin is obtained from the γ-isomer. F. Wessely, K. Schlögl, and E. Wawersich, M. *84*, 263 (1953); degradation of peptides s. other papers of this series.

Neber-Bossel 3-hydroxycinnoline ring synthesis

569. 

o-Nitromandelic acid neutralized with 2.1 *N* NaOH, dil. with water. hydrogenated with 5%-Pd-charcoal for 4 hrs., filtered, the Na-o-aminomandelate (Y of the free acid, when isolated: 85%) soln. concd. to ca. half its volume, treated with $NaNO_2$, the resulting soln. added dropwise at 0° to stirred concd. HCl (the acid cannot be diazotized directly because of the rapidity with which dioxindole is formed), stirring continued for a few min., after removal of the freezing bath, then added slowly at 0° to $SnCl_2$ and concd. HCl, slow stirring continued ¾ hr. at room temp., the resulting "tin salt" decomposed with H_2S, and the product boiled 0.5 hr. in HCl → 3-hydroxycinnoline. Y: 59.5-61.2%. F. e. s. E. J. Alford and K. Schofield, Soc. *1952*, 2102.

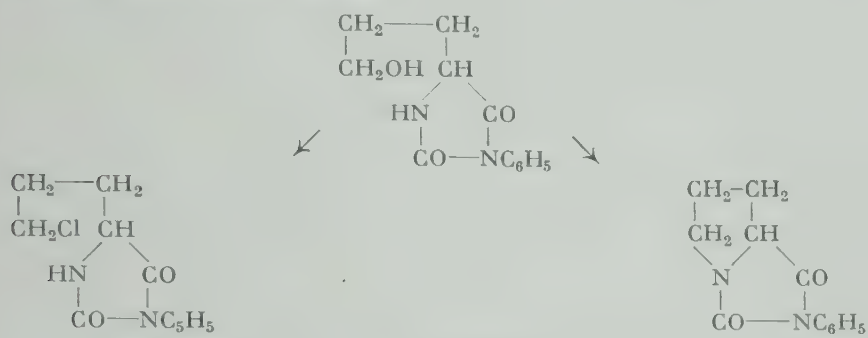
Pyrrolo(2′3′:3,4)isocoumarins as intermediates
s. *9*, 740

1,3,4-Thiadiazines from α-(dithiocarbazyl)oxo compounds
s. *9*, 697

Hydrobromic acid *HBr*

Different reactivity of halides

570.



3-Phenyl-5-γ-hydroxypropylhydantoin (prepn. s. 404)

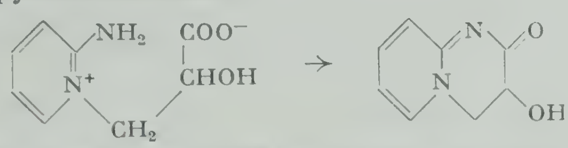
treated at 125° with dry HCl-gas for 2 hrs. → 3-phenyl-5-γ-chloropropylhydantoin. Y: 77%.

heated with 48%-HBr 2 hrs. at 90° → 3-phenyl-1,5-trimethylenehydantoin. Y: 71%.

R. Gaudry, Can. J. Chem. *29*, 544 (1951); different reactivity of halides s. a. Synth. Meth. *7*, 567.

Pyrido[1,2-a]pyrimidin-2-ones

571.

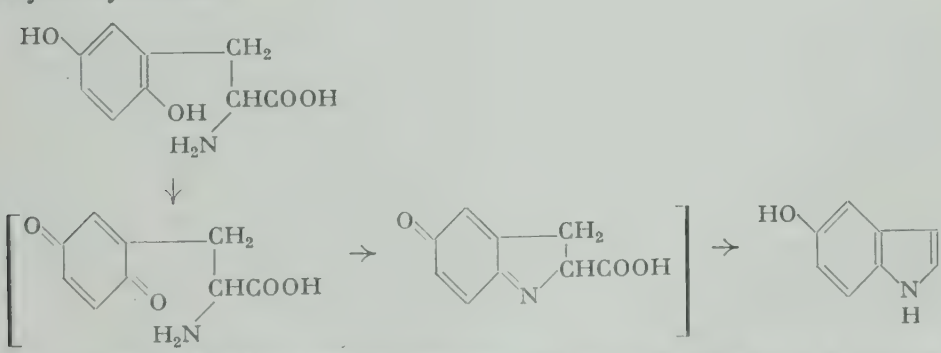


48%-HBr added to 2-imino-1(2H)-pyridinelactic acid in water, and evaporated to dryness at room temp. under a stream of air → 3,4-dihydro-3-hydroxy-2H-pyrido[1,2a]pyrimidin-2-one hydrobromide. Y: 100%. R. Adams and I. J. Pachter, Am. Soc. *74*, 4906 (1952).

Potassium ferricyanide *$K_3[Fe(CN)_6]$*

Hydroxyindoles

572.



An aq. soln. of K-ferricyanide and $NaHCO_3$ added with stirring during 10 min. to an aq. soln. of 2,5-dihydroxyphenylalanine monohydrate and

$NaHCO_3$, extracted with peroxide-free ether when the color has become pale yellow → 5-hydroxyindole. Y: 85%.—Similarly from 2,5-dihydroxy-β-phenylethylamine. Y: 70%. R. I. T. Cromartie and J. Harley-Mason, Soc. *1952*, 2525; *1954*, 1165.

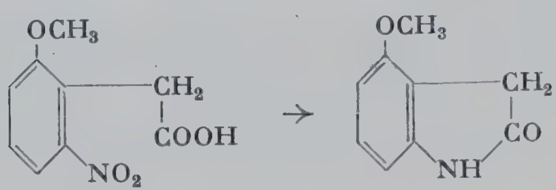
Nickel *Ni*

Quinolizidines

s. *5*, 365; s. a. K. Winterfeld and E. Müller, A. *581*, 77 (1953)

Palladium *Pd*

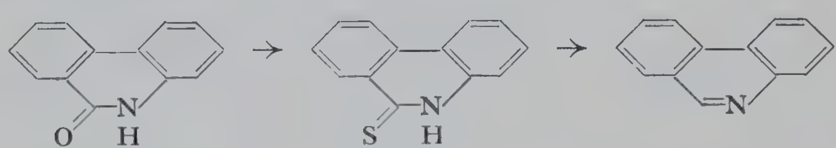
Reductive ring closure to N-heterocyclics

573. 

0.5 g. 2-methoxy-6-nitrophenylacetic acid hydrogenated with Pd-black in glacial acetic acid at room temp. → 0.38 g. 4-methoxyoxindole. J. W. Cook, J. D. Loudon, and P. McCloskey, Soc. *1952*, 3904.

Via intermediates *v.i.*

Phenanthridines from phenanthridones via phenanthrithiones ←

574. 

A mixture of phenanthridone, P_2S_5, and pyridine refluxed 2 hrs. → phenanthridinethione (Y: 94%) refluxed with Raney-Ni in dimethylformamide-ethanol → phenanthridine (Y: 95%). E. C. Taylor, Jr., and A. E. Martin, Am. Soc. *74*, 6295 (1952).

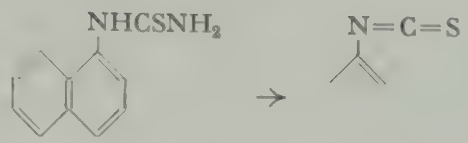
Nitrogen ↑ NC ⇑ N

Without additional reagents *w.a.r.*

Acylamines from carboxylic acid azides $CON_3 \rightarrow NHAc$

s. *3*, 408; in benzene without acetic acid s. M. B. Moore et al., Am. Soc. *76*, 3656 (1954)

Arylisothiocyanates from arylthioureas $NHCSNH_2 \rightarrow N{:}C{:}S$

575. 

α-Naphthylthiourea heated 8 hrs. in chlorobenzene at 150° → α-naphthylisothiocyanate. Y: 91.5% based on startg. m. consumed. F. e. s. J. N. Baxter et al., Chem. & Ind. *1954*, 785.

Irradiation ← .

Isatogens from quaternary cyclic hydroxyammonium salts ○

s. *9*, 733

Iron *Fe*

Indoles

s. *5*, 368; s. a. A. Ek and B. Witkop, Am. Soc. *76*, 5579 (1954)

Halogen ↑ NC ⇑ Hal

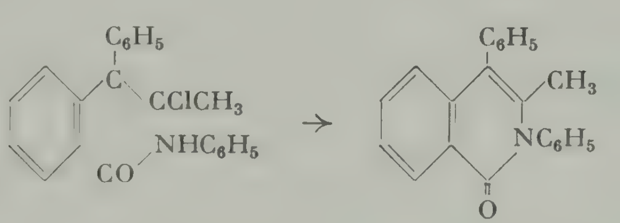
Potassium hydroxide *KOH*

2-Oxazolidones from halogenourethans ○

s. *9*, 45

Potassium hydroxide/alcohol

Isocarbostyrils

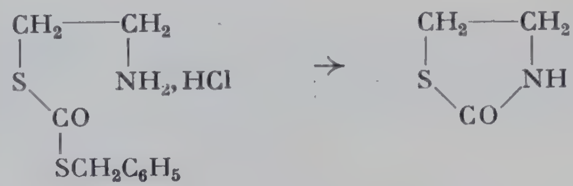
576. 

0.356 g. o-(1-phenyl-2-chloropropenyl)benzoic acid anilide treated with alc. 8%-KOH, and refluxed 3 hrs. → 0.302 g. 2.4-diphenyl-3-methylisocarbostyril. F. e. s. G. Berti, G. *81*, 868 (1951).

Sulfur ⇞ NC ⇑ S

Sodium hydroxide *NaOH*

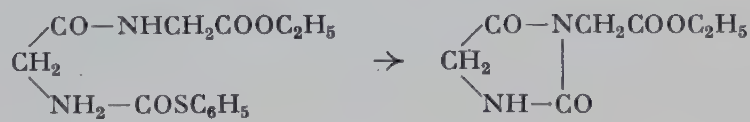
2-Thiazolidones from dithiolcarbonic acid esters

577. 

N NaOH added to a suspension of 2-aminoethyl benzyl dithiolcarbonate hydrochloride (prepn. s. 705) in ethanol, and kept 3 hrs. in a stoppered flask → 2-ketothiazolidine. Y: 98%. F. e. s. J. C. Crawhall and D. F. Elliott, Soc. *1952*, 3094.

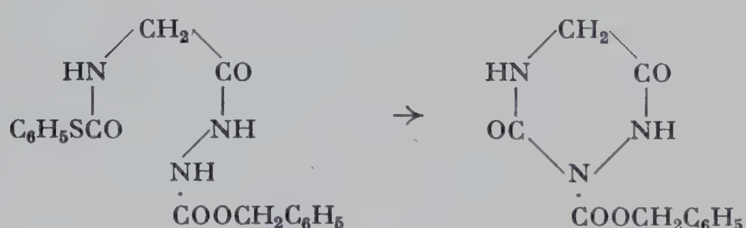
Lead acetate *$(CH_3COO)_2Pb$*

Hydantoins from N-thiocarbonyldipeptides

578. 

Phenylthiocarbonyldiglycine ethyl ester added to a warm soln. of Pb-acetate in 70%-ethanol, and heated 5 min. at 80-85° → ethyl hydantoin-3-acetate. Y: 82%. F. e. s. A. Lindenmann, N. H. Khan, and K. Hofmann, Am. Soc. *74*, 476 (1952); s. a. F. Wessely, K. Schlögl, and E. Wawersich, M. *83*, 1439 (1952).

1,2,4-Triazines

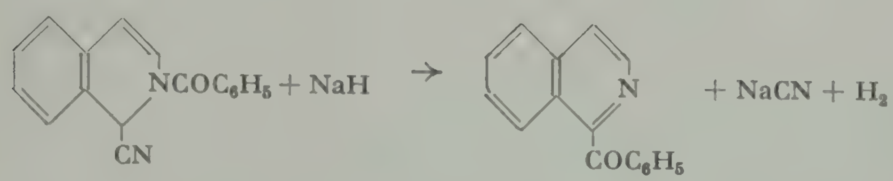
579. 

Phenylthiocarbonylglycine carbobenzoxyhydrazide added to a warm soln. of Pb-acetate in 70%-alcohol, and heated 6 min. at 80-85° → 2-carbobenzoxy-3,6-dioxohexahydro-1,2,4-triazine. Y: 78%. A. Lindenmann, N. H. Khan, and K. Hofmann, Am. Soc. *74*, 476 (1952).

Carbon ↓ NC ⇑ C

Sodium hydride *NaH*

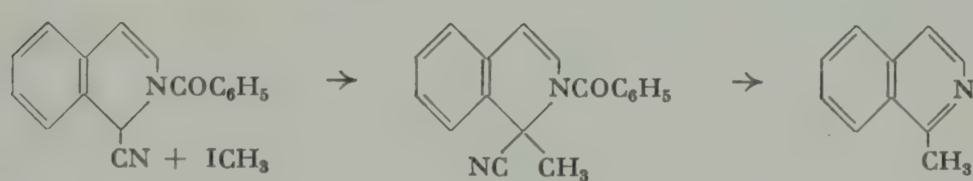
Rearrangement of Reissert compounds to o-acyl-N-heterocyclics ←

580. 

A mixture of 1-cyano-2-benzoyl-1,2-dihydroisoquinoline, NaH, and dry xylene refluxed with stirring until the expected amount of H_2 is evolved. then heated an additional 2 hrs. on a steam bath → 1-benzoylisoquinoline. Y: 70%. F. e. s. V. Boekelheide and J. Weinstock, Am. Soc. *74*, 660 (1952).

Potassium hydroxide *KOH*

o-Alkyl-N-heterocyclics from Reissert compounds ←

581. 

Ethereal phenyl-Li added dropwise at -10^0 under N_2 with stirring to a soln. of 1-cyano-2-benzoyl-1,2-dihydroisoquinoline, then methyl iodide added slowly, stirred 2 hrs. in the cold and overnight at room temp. → 2-benzoyl-1-cyano-1-methyl-1,2-dihydroisoquinoline (Y: 72%) dissolved in ethanol, added to aq. KOH, and refluxed 0.5 hr. → 1-methylisoquinoline (Y: 80%). F. e. s. V. Boekelheide and J. Weinstock, Am. Soc. *74*, 660 (1952); second step with aq. 33%-H_2SO_4 s. J. Org. Chem. *19*, 587 (1954).

Magnesium *Mg*

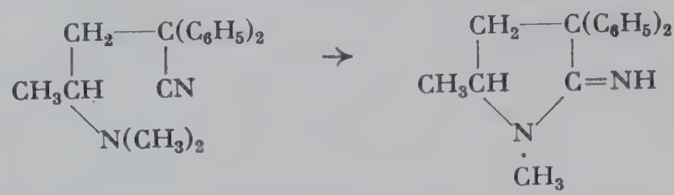
Imidazole ring closure ○

imidazolines s. *3*, 415; imidazolo(5′,4′:2,3)pyridines s. F. Korte, B. *85*. 1012 (1952)

Ammonium benzenesulfonate *$C_6H_5SO_3NH_4$*

Pyrrolidines from tert-aminonitriles

582.



A mixture of 3-dimethylamino-1,1-diphenylbutyl cyanide and NH_4-benzenesulfonate heated 4 hrs. at 255-260°, and the product isolated as the hydrochloride → 2-imino-1,5-dimethyl-3,3-diphenylpyrrolidinium chloride. Y: 50%. J. Cymerman and W. S. Gilbert, Soc. *1952*, 3529; with concd. HCl s. W. Wilson, Soc. *1952*, 3524.

Sulfuric acid *H_2SO_4*

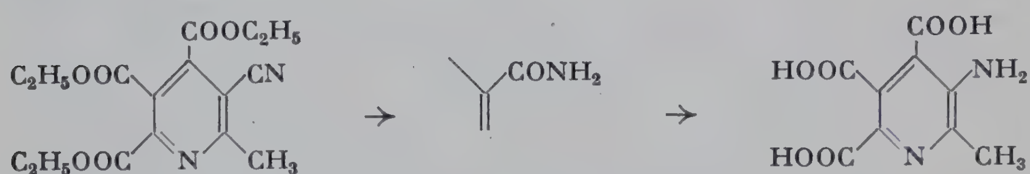
o-Alkyl-N-heterocyclics from Reissert compounds ←

s. *9*, 581

Sodium hypochlorite *NaOCl*

Amines from nitriles via carboxylic acid amides Hofmann degradation CN → NH_2

583.



97%-H_2SO_4 added with vigorous stirring and cooling to triethyl 5-cyano-6-methyl-2,3,4-pyridinetricarboxylate, and kept 1 hr. at 35-40° with occasional cooling → triethyl 5-carbamyl-6-methyl-2,3,4-pyridinetricarboxylate (Y: 89-95%) added with stirring to a mixture of ice and aq. NaOH into which Cl_2 has been introduced, after 1 hr. when the mixture has reached room temp. heated on a steam bath for 0.5 hr., 12 *N* HCl added slowly with stirring, and the mixture which should be about pH 2 kept 60 hrs. at 0° → 5-amino-6-methyl-2,3,4-pyridinetricarboxylic acid. Y: 87-91%. R. G. Jones, Am. Soc. *73*, 5610 (1951).

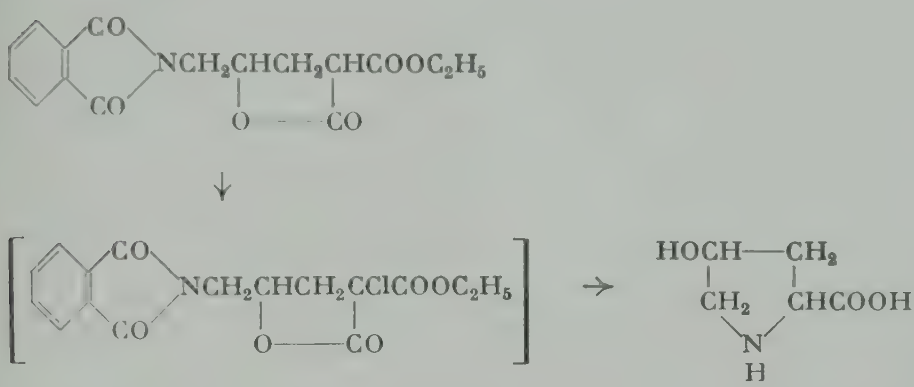
Hydrochloric acid *HCl*

Pyrrolidines from tert-aminonitriles ○

s. *9*, 582

Via intermediates *v.i.*

4-Hydroxypyrrolidine-2-carboxylic acids ←
Halogenation

584. 

SO_2Cl_2 added dropwise with stirring to a soln. of 2-carbethoxy-5-phthalimido-4-valerolactone in glacial acetic acid, heated 2 hrs. at 70°, evaporated to dryness in vacuo, washed with water, glacial acetic acid and concd. HCl added, refluxed 3 hrs., again evaporated to dryness under reduced pressure, dissolved in water, phthalic acid filtered off, the filtrate treated with $Ba(OH)_2$, refluxed 6 hrs., and the product isolated as the Cu-salt → hydroxyproline Cu-salt (Y: 36.4%) and allo-hydroxyproline Cu-salt (Y: 36.4%). F. syntheses s. R. Gaudry and C. Godin, Am. Soc. *76*, 139 (1954).

Formation of Hal—Hal Bond

Uptake

Addition to Halogen HalHal ⇓ Hal

Sodium chloride *NaCl*

Sulfonium polyhalides ←

585. $$(C_6H_5)_3S^+\ Br^- + Cl_2 \rightarrow (C_6H_5)_3S^+\ BrCl_2^-$$

An aq. soln. of triphenylsulfonium bromide and NaCl treated with Cl-water → triphenylsulfonium dichlorobromide. Y: 78%. F. e. s. W. A. Bonner, Am. Soc. *74*, 5078 (1952).

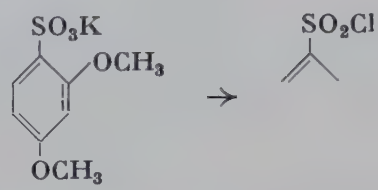
Formation of Hal—S Bond

Exchange

Oxygen ↑ HalS ⇅ O

Phosphorus oxychloride *$POCl_3$*

Sulfonic acid chlorides $SO_3K \rightarrow SO_2Cl$

586. 

from potassium sulfonates. Dried crude K-2,4-dimethoxybenzenesulfonate pulverized and treated under reflux with $POCl_3$ for 1.5 hrs. → 2,4-dimethoxybenzenesulfonyl chloride. Y: 88%. H. R. Snyder and R. E. Heckert, Am. Soc. *74*, 2006 (1952).

Phosphorus pentachloride *PCl_5*

from sodium sulfonates $SO_3Na \rightarrow SO_2Cl$

s. *9*, 392; s. a. C.S. Rondestvedt, Jr., and F.G. Bordwell, Org. Synth. *34*, 85 (1954)

Sulfur ↑ HalS ⇅ S

Without additional reagents *w.a.r.*

Sulfur trichlorides from disulfides $RSSR \rightarrow 2\,RSCl_3$

587. $$CH_3S \cdot SCH_3 + 3\,Cl_2 \rightarrow 2\,CH_3SCl_3$$

A gentle stream of Cl_2 passed through an inlet tube which terminates just above the surface of methyl disulfide dil. with methylene chloride and cooled to –25 to –20° → methylsulfur trichloride. Y: almost 100%. K. R. Brower and I. B. Douglass, Am. Soc. *73*, 5787 (1951).

Carbon ↑ HalS ⇅ C

Without additional reagents *w.a.r.*

Anhydrous chlorination of thiocarboxylic acid esters and related compounds ←

588. $$CH_3OCSSCH_3 \rightarrow CH_3OC(Cl_2)SCl$$

Anhydrous Cl introduced into a soln. of methyl methylxanthate in liq. butane in a bath containing Dry Ice and acetone until no more solid is

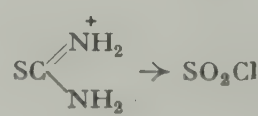
formed, centrifuged, and the centrifugate again chlorinated to cause any ester previously trapped in the solid to react → methoxydichloromethanesulfenyl chloride. Y: 70%. F. e. s. I. B. Douglass and C. E. Osborne, Am. Soc. *75*, 4582 (1953).

Chlorine *Cl*

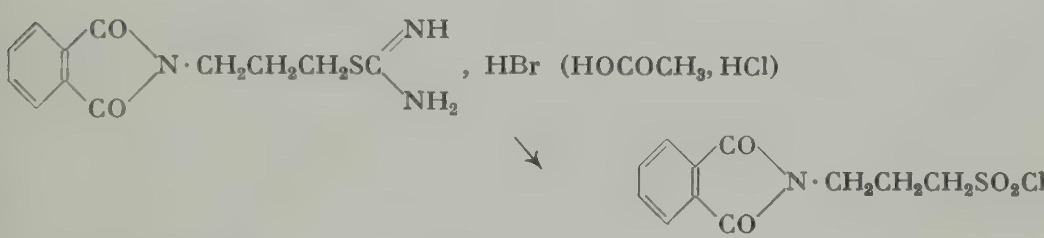
Sulfonic acid chlorides from thiocyanates SCN → SO_2Cl

s. *4*, 469; s. a. A. P. Terent'ev and A. I. Gershenovich. Ж. *23*, 204 (1953); C. A. *48*, 2568i

Sulfonic acid chlorides from isothiouronium salts



589.



A hot satd. aq. soln. of K-acetate added with stirring at 80° to a hot aq. soln. of 105 g. S-(3-phthalimidopropyl)thiouronium bromide, the resulting thiouronium acetate suspended in water, concd. HCl added, then Cl passed in at 0-5° for 3 hrs. → 64 g. 3-phthalimido-1-propanesulfonyl chloride.—Alkyl bromides react more readily with thiourea than alkyl chlorides (cf. Synth. Meth. *1*, 493, 495; *3*, 520), and therefore thiouronium bromides are used as intermediates. F. e. s. W. Griffin and D. H. Hey, Soc. *1952*, 3334.

Formation of Hal—Rem Bond

Uptake

Addition to Remaining Elements HalRem ⇓ Rem

Without additional reagents *w.a.r.*

Selenium dihalides from selenides >Se → >$SeHal_2$

dibromides s. *6*, 539; also dichlorides s. H. Rheinboldt and M. Perrier. Bl. *1953*, 379

Exchange

Oxygen ↑ HalRem ⇅ O

Without additional reagents *w.a.r.*

Halogeno- from alkoxy-silanes ←

590. $(n{-}C_3H_7)_2Si(OC_2H_5)_2 + 2\,HF \rightarrow (n{-}C_3H_7)_2SiF_2$

A mixture of di-n-propyldiethoxysilane and 48%-HF stirred 3 hrs. at 0° in a copper flask → di-n-propyldifluorosilane. Y: 95.5%. F. e. s. N. S. Marans, L. H. Sommer, and F. C. Whitmore, Am. Soc. *73*, 5127 (1951).

Fluorosilanes
s. *9*, 592

Chlorotitanium alkoxides ←

591. $(n{-}C_3H_7O)_4Ti + CH_3COCl \rightarrow (n{-}C_3H_7O)_3TiCl + CH_3COOC_3H_7{-}n$

1 molar equivalent acetyl chloride added slowly with stirring and water cooling to tetra-n-propyl titanate, refluxed 3 hrs., the propyl acetate formed distilled off at ordinary pressure, then the product distilled at reduced pressure → chlorotitanium tri-n-propoxide. Y: 90%. F. e. s. N. M. Cullinane et al., J. Applied Chem. *2*, 250 (1952).

Sodium chloride *NaCl*

Chloro- from aceto-mercury compounds HgOAc → HgCl
s. *9*, 712

Halogen ↑ HalRem ⇅ Hal

Without additional reagents *w.a.r.*

Fluorosilanes SiF

592. $(C_2H_5)_3SiCl \rightarrow (C_2H_5)_3SiF$

$$(C_6H_5)_3SiOC_2H_5 \rightarrow (C_6H_5)_3SiF$$

Chlorotriethylsylane allowed to react 2 hrs. with HF in alcohol at 75° → fluorotriethylsilane. Y: 85%.—Similarly: Ethoxytriphenylsilane 24 hrs. at 18° → fluorotriphenylsilane. Y: ca. 100%. F. e., also from silanols, disiloxanes, and bromosilanes, s. C. Eaborn, Soc. *1952*, 2846.

Sulfur ↑ HalRem ⇅ S

Silver salt *Ag⁺*

Conversion series ←

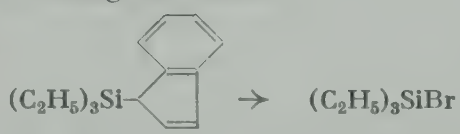
Organosilicon compounds s. 7, 545; extension s. H. H. Anderson and H. Fischer, J. Org. Chem. *19*, 1296 (1954); organotin compounds s. H. H. Anderson and J. A. Vasta. J. Org. Chem. *19*, 1300 (1954)

Carbon ↑ HalRem ⇅ C

Without additional reagents *w.a.r.*

Cleavage of silanes to halogenosilanes SiR → SiHal

593.



Br added slowly with stirring to 1-(triethylsilyl)indene → triethylbromosilane. Y: 83.1%. F. e. s. L. H. Sommer and N. S. Marans, Am. Soc. *73*, 5135 (1951); s. a. J. J. McBride, Jr., and H. C. Beachell, Am. Soc. *74*, 5247 (1952).

Hydrochloric acid *HCl*

Monoalkyl from dialkyl mercury compounds $RHgR' \rightarrow RHgCl$

594. $$C_2H_5HgCH_2CH{=}CH_2 \rightarrow C_2H_5HgCl$$

An ethereal soln. of allylethylmercury (prepn. s. 723) warmed with alcohol satd. with HCl → ethyl-HgCl. Y: 70%. E. Rothstein and R. W. Saville, Soc. *1952*, 2987.

Formation of Hal—C Bond

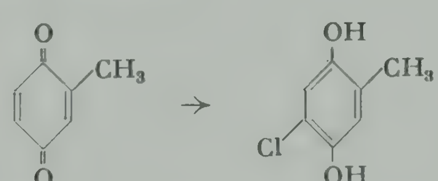
Uptake

Addition to Oxygen and Carbon HalC ⇓ OC

Without additional reagents *w.a.r.*

Halogenoquinols from quinones ←

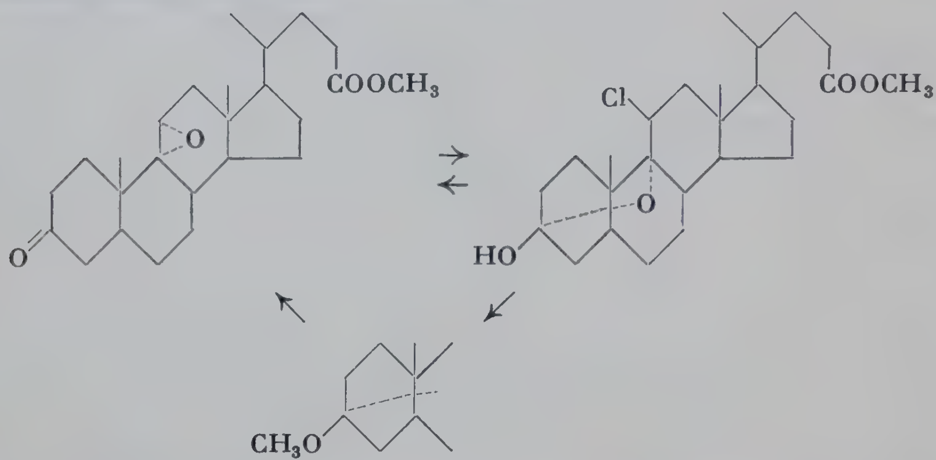
595.



Dry HCl passed slowly into a soln. of 2,5-toluquinone in chloroform at room temp. with water-cooling for 1 hr. → 4-chloro-2,5-toluquinol.

Y: 80%. H. Burton and D. F. G. Praill, Soc. *1952*, 755; from o-quinones s. R. R. Holmes et al., Am. Soc. *76*, 2400 (1954).

Halogenolactols from oxidoketones ←
and reverse reaction
Lactolides from lactols
Oxidoketones from halogenolactolides

596. 

Dry HCl passed for 15 min. into a soln. of methyl 3-keto-9α,11α-oxidocholanate (prepn. s. 361) in alcohol-free chloroform, and allowed to stand for an additional 20 min. → methyl 3β-hydroxy-3α,9α-oxido,11β-chlorocholanate (startg. m. f. 272) (Y: 96%)

dissolved in methanol, 0.1 *N* NaOH and a drop of phenolphthalein soln. added, then refluxed ca. 5 min. until the color disappears (Y: 79%)

a hot soln. of which in 0.1 *N* methanolic HCl boiled 5 min. → methyl 3β-methoxy-3α,9α-oxido-11β-chlorocholanate (Y: 77.5%) dissolved in glacial acetic acid, added to Ag-acetate, and warmed 40 min. on a steam bath with occasional agitation (Y: 91%)

↘ ↙

methyl 3-keto-9α,11α-oxidocholanate

F. e., lactolides also with 48%-HBr, s. H. Heymann and L. F. Fieser, Am. Soc. *73*, 5252 (1951).

Sulfuric acid H_2SO_4

Dibromides from cyclic ethers C

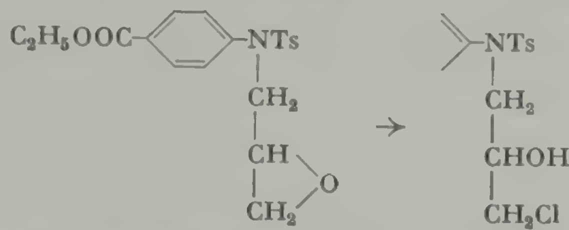
597. 

Concd. H_2SO_4 added cautiously to a stirred soln. of tetrahydrosylvan in 40%-HBr heated on a steam bath, heating and stirring continued for 3.5 hrs. → 1,4-dibromopentane. Y: 80%. N. J. Leonard and J. Figueras, Jr., Am. Soc. *74*, 917 (1952).

Pyridine hydrochloride *C_5H_5N,HCl*

Halogenhydrins from oxido compounds C—C(—O—) → C(OH)CHal

8.



A soln. of ethyl N-tosyl-N-(2,3-oxidopropyl)-p-aminobenzoate and pyridine hydrochloride in ethanol-water refluxed 30 min. → ethyl N-tosyl-N-(3-chloro-2-hydroxypropyl)-p-aminobenzoate. Y: 72.6%. D. I. Weisblat et al., Am. Soc. *75*, 3625 (1953).

Addition to Nitrogen and Carbon HalC ⇓ NC

Without additional reagents *w.a.r.*

Imine ring opening
s. *4*, 478; s. a. Am. Soc. *74*, 4451 (1952)

Halogenocyanamides from cyclic imines

99. cf. Synth. Meth. *6*, 552
The direction of ring opening varies with the substituent on the nitrogen. E., also side reactions, s. R. C. Elderfield and M. Green, J. Org. Chem. *17*, 431 (1952).

Addition to Carbon HalC ⇓ CC

Without additional reagents *w.a.r.*

1,2-Dibromides from ethylene derivatives C:C → CBrCBr
s. *9*, 899, 928

1,2-Nitrochlorides from ethylene derivatives $C{:}C \rightarrow CClC(NO_2)$
s. *6*, 558; at elevated temp. s. R. N. Haszeldine, Soc. *1953*, 2075

2-Iodoacetals from enol acetates $C{:}C(OAc) \rightarrow CIC(OR)_2$

00. $CH_2{=}CHOCOCH_3 \rightarrow [ICH_2CHCl(OCOCH_3)] + 2\,C_2H_5OH \rightarrow ICH_2CH(OC_2H_5)_2$

A mixture of concd. HCl and ICl added below 5° with gentle stirring to a soln. of vinyl acetate in CCl_4 until, after 20 min., ICl is no longer decolorized, the lower organic layer separated rapidly, added to a mixture of 99.5-100%-ethanol and $CaCl_2$, then allowed to stand 3 days at 10-15° → iodoacetaldehyde diethyl acetal. Y: 82-85%. S. Akiyoshi and K. Okuno, Am. Soc. *74*, 5759 (1952).

1,1,2-Trichlorides from ethylene derivatives ←
via chlorohydrins and α,β-ethylenechlorides

601. $CH_3CH{=}CHCHO \rightarrow [CH_3CH(OH)CHClCHO \downarrow CH_3CH{=}CClCHO] \rightarrow CH_3CHClCCl_2CHO$

Cl-gas introduced into a stirred mixture of crotonaldehyde and water at ca. 10° for ca. 2 hrs. until the temp. does not rise rapidly when the bath is removed, then refluxed 30 min. with slow stirring to dehydrate the chlorohydrin, the α-chlorocrotonaldehyde obtained extracted with chloroform (can be isolated in high yields from this extract), treated at 0-10° with chlorine until 1 mole has been added, stirred 1 hr. longer in the ice bath, and dry CO_2 or N_2 bubbled through the soln. at room temp. to remove excess Cl_2 → α,α,β-trichlorobutyraldehyde. Y: 52-53%. G. A. Ropp, W. E. Craig, and V. Raaen, Org. Synth. *33*, 15 (1953).

Halogenosteroids from 3,5-cyclosteroids C
s. *9*, 635

Irradiation ←

Bromides from ethylene derivatives C:C → CHCBr
Free radical additions

602. $CF_3CH{=}CH_2 + HBr \rightarrow CF_3CH_2CH_2Br$

Trifluoropropene and dry HBr irradiated 18 hrs. at room temp. with UV-light in a sealed silica tube → 3-bromo-1,1,1-trifluoropropane. Y: 97%. No addition takes place in the dark. F. e. s. R. N. Haszeldine, Soc. *1952*, 2504, 3490; s. a. A. L. Henne and M. Nager, Am. Soc. *73*, 5527 (1951).

Ethylene from acetylene derivatives ←
via 1,2-dibromides
Deutero compounds

603. $DC{\equiv}CD + 2\,DBr \rightarrow CD_2BrCD_2Br \rightarrow CD_2{=}CD_2$

A 2:1 mixture of DBr (from D_2O and PBr_3) and acetylene-d_2 containing a little air allowed to react at atmospheric pressure, whereby the reaction sets in after a variable induction period or irradiation for a few. min. with UV-light → 1,2-dibromoethane-d_4 (Y: almost 100%) in dioxane added slowly with stirring to Zn-dust and a crystal of NaI, heated gently at first, then gradually to reflux → ethylene-d_4 (Y: 80-86%). L. C. Leitch and A. T. Morse, Can. J. Chem. *30*, 924 (1952).

Sodium acetate *CH_3COONa*

1,2-Dibromides from ethylene derivatives C:C → CBrCBr
s. *9*, 362

Magnesium oxide *MgO*

1,2-Alkoxyhalides from ethylene derivatives C:C → C(OR)CHal

604. $(CH_3)_2C{=}CHCOOH \rightarrow (CH_3)_2C(OCH_3){-}CH(Br)COOH$

Br_2 introduced at 10° by means of a current of dried air into a well-stirred mixture of β.β-dimethylacrylic acid, methanol. and finely powdered MgO over a period of 4.5 hrs., and stirring continued for 15 min. until the mixture becomes colorless → α-bromo-β-methoxyisovaleric acid. Crude Y: 75%. K. Rüfenacht, Helv. *35*, 762 (1952).

Aluminum halide *$AlHal_3$*

Addition of hydrogen halides to acetylene derivatives ←

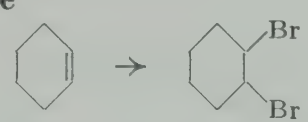
605. $CF_3C{\equiv}CH + HI \rightarrow CF_3CH{=}CHI$

Trifluoropropyne and anhydrous HI allowed to react at room temp. in the presence of AlI_3 → 3,3.3-trifluoro-1-iodopropene. Y: 80%. F. e. s. R. N. Haszeldine, Soc. *1952*, 3490.

N-Bromosuccinimide and tetraethylammonium bromide ←

Reaction between ethylene derivatives and N-bromosuccinimide ←

606.



Normally, allylic substitution is predominant, but certain structural features and catalysts promote addition to form satd. 1,2-dibromides.– E: A mixture of cyclohexene, N-bromosuccinimide, tetraethylammonium bromide, and chloroform refluxed 20 min. → 1,2-dibromocyclohexane. Y: 74%. F. e. s. E. A. Braude and E. S. Waight, Soc. *1952*, 1116.

Sulfuryl chloride *SO_2Cl_2*

Halogenolactones ←
Lactones from halogenocarboxylic acid esters with simultaneous replacement of carbalkoxy groups by hydrogen
Trihalides from ethylene derivatives

607. $CH_2{=}CHCH_2CH(COOC_2H_5)_2 \rightarrow ClCH_2CHClCH_2CCl(COOC_2H_5)_2$

$\downarrow$

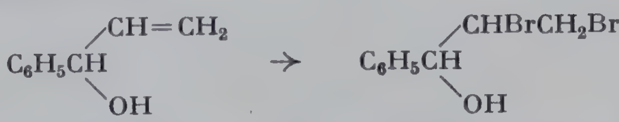
$ClCH_2\underset{|}{C}HCH_2\underset{|}{C}HCl$ (O——CO) $\leftarrow$ $[ClCH_2\underset{|}{C}HCH_2\underset{|}{C}ClCOOH$ (O——CO)$]$

SO_2Cl_2 added dropwise to cooled diethyl allylmalonate, stirred 1 hr. at room temp., refluxed 20 min., excess SO_2Cl_2 evaporated under re-

duced pressure, the crude ethyl 2-carbethoxy-2,4,5-trichlorovalerate dissolved in glacial acetic acid, HCl added, and refluxed 3 hrs. → 2,5-dichloro-4-valerolactone. Y: 90.5%. F. e., also mixed dihalogenovalerolactones by stepwise introduction of halogen, s. R. Gaudry and C. Godin, Am. Soc. *76*, 139 (1954).

Pyridine hydrobromide perbromide *$C_5H_5N,HBr \cdot Br_2$*

1,2-Dibromo-3-alcohols from 2-ethylenealcohols C:C → CBrCBr

608. 

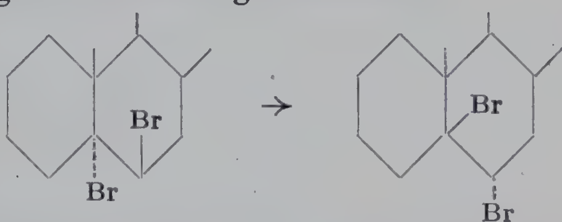
Pyridine hydrobromide perbromide added portionwise at 12-15° with stirring to a soln. of (±)-1-phenylallyl alcohol in glacial acetic acid, and worked up after 45 min. → (±)-2,3-dibromo-1-phenylpropanol. Y: 47%.—Use of free bromine was unsuccessful. Also with the (±)-compound s. C. L. Arcus and H. E. Strauss, Soc. *1952*, 2669.

Rearrangement

Hydrogen/Carbon Type HalC ⟲ HC

Sodium acetate *CH_3COONa*

Change in configuration of halogenosteroids ←

609. 

A soln. of 5α,6β-dibromocholestane in glacial acetic acid and chloroform containing Na-acetate kept 8 hrs. at ca. 40° in a closed flask → 5β,6α-dibromocholestane. Y: 75-6%. C. A. Grob and S. Winstein, Helv. *35*, 782 (1952).

Exchange

Hydrogen ↓ HalC ⇅ H

Without additional reagents *w.a.r.*

Halogenofuranones from acoxyfurans ←

610. 

Br in CCl_4 added at −5 to −10° during 8 min. to a stirred soln. of 2-acetoxyfuran in CCl_4 → 5-bromo-2(5H)-furanone. Y: 81%. Also chloro

derivatives s. N. Elming and N. Clauson-Kaas. Acta Chem. Scand. *6*, 565 (1952).

Irradiation ←

Directed halogenation H → Hal

Photochlorination of aliphatic compounds

611. $CH_3CH_2CN \rightarrow ClCH_2CH_2CN$

$CH_3CH_2CH_2OCOCH_3 \rightarrow CH_3CHClCH_2OCOCH_3$

Nitriles, esters, acid chlorides, and alkyl acetates, in which the α-C-atom is generally deactivated for photochlorination, are chlorinated in the *vapor phase*. This procedure gives reproducable yields and reduces polychlorinated products to a minimum. Acids are chlorinated in the liquid phase to avoid dehydrochlorination.—E: Propionitrile chlorinated in the vapor phase with irradiation → β-chloropropionitrile (Y: ca. 65%) and α-chloropropionitrile (Y: ca. 21%).—Similarly: Propyl acetate → β-chloropropyl acetate (Y: ca. 50%) and γ-chloropropyl acetate (Y: ca. 20%). F. e. s. A. Bruylants et al., Bull. soc. chim. Belg. *61*, 366 (1952); α-chlorination of ketones s. *61*, 492; α-bromination of nitriles s. J. Org. Chem. *18*, 501 (1953).

Bromination H → Br

s. *1*, 410, 418; s. a. J. C. Bill and D. S. Tarbell, Org. Synth. *34*, 82 (1954); E. F. M. Stephenson, Org. Synth. *34*, 100;
1,2-dibromides s. *9*, 972; polybromination of steroids s. H. H. Inhoffen, H. Jahnke, and P. Nehring, B. *87*, 1154 (1954)

Sodium acetate *CH_3COONa*

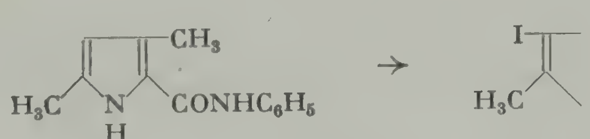
1,1,1-Trihalides $CH_3 \rightarrow CHal_3$

s. *3*, 155; *7*, 560; s. a. R. Roth and H. Erlenmeyer, Helv. *37*, 1064 (1954)

Potassium iodide *KI*

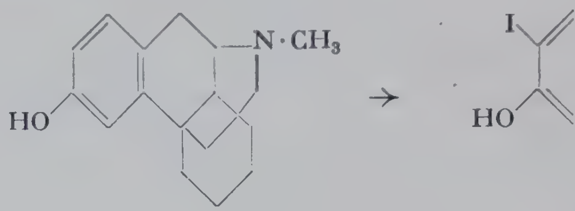
Iodination H → I

612.



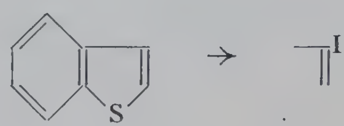
2,4-Dimethylpyrrole-5-carboxylic acid anilide dissolved in hot alcohol-water, and treated with a soln. of iodine in K-iodide → 3-iodo-2,4-dimethylpyrrole-5-carboxylic acid anilide. Y: 88%. A. Treibs and W. Ott. A. *577*, 119 (1952).

Potassium iodide/sodium hydroxide *KI/NaOH*

613. 

An aq. soln. of KI and iodine added dropwise with stirring to a soln. of 3-hydroxy-N-methylmorphinane in aq. NaOH, and stirring continued for 15 min. → 3-hydroxy-2-iodo-N-methylmorphinane. Y: 85%. R. Grewe, A. Mondon, and E. Nolte, A. *564*, 161 (1949); s. a. H. Lettré, H. Fernholz, and E. Hartwig, A. *576*, 147 (1952); D. Papa et al., Am. Soc. *75*, 1107 (1953); 4-halogeno-5-pyrazolones s. G. Westöö, Acta Chem. Scand. *6*, 1499 (1952).

Mercuric oxide *HgO*

614. 

Yellow mercuric oxide and iodine added alternately in small portions during 1 hr. at 55-65° to a soln. of thianaphthene in benzene → 3-iodothianaphthene. Y: 71% based on converted startg. m. R. Gaertner, Am. Soc. *74*, 4950 (1952).

Dioxane ←

Bromination H → Br

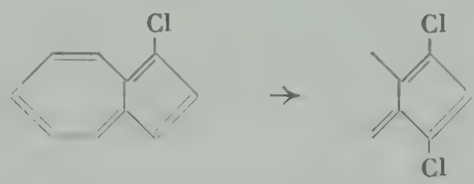
615. 

The dioxane-bromine complex is suitable for mild direct halogenation of sensitive ar. compounds.–E: Br in dioxane added dropwise during 2 hrs. with good agitation at 5° to a soln. of aniline in dioxane and aq. KOH → p-bromoaniline. Y: 68%. F. e. s. G. M. Kosolapoff, Am. Soc. *75*, 3596 (1953); phenols s. L. A. Yanovskaya, A. P. Terent'ev, and L. J. Belen'kiĭ, Ж. *22*, 1594 (1952); C. A. *47*, 8032 h; aldehydes and ketones s. Ж. *22*, 1598; C. A. *47*, 9258e; J. D. Billimoria and N. F. Maclagan. Soc. *1954*, 3257.

N-Halogenosuccinimide $\begin{matrix}CH_2CO\\ \vert\\ CH_2CO\end{matrix}\rangle NHal$

Halogenation H → Hal

16.



Azulenes. A soln. of N-chlorosuccinimide in dry benzene added to a soln. of 1-chloroazulene in petroleum ether, and the product isolated after 12 hrs. when the test with starch-iodide paper is negative → 1,3-dichloroazulene. Net Y: 82%. F. e. and brominations with N-bromosuccinimide s. A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, Am. Soc. *75*, 4980 (1953).
Chlorination of pyrimidines s. R. A. West und H. W. Barrett, Am. Soc. *76*, 3146 (1954).

N-Bromosuccinimide $\begin{matrix}CH_2CO\\ \vert\\ CH_2CO\end{matrix}\rangle NBr$

Halogenation
s. *9*, 640

Directed halogenation
s. *9*, 611

Bromination
s. *9*, 927

1,1-Bromonitro compounds from oximes ←
s. *9*, 168

N-Bromosuccinimide/tetraethylammonium bromide $\begin{matrix}CH_2CO\\ \vert\\ CH_2CO\end{matrix}\rangle NBr/(C_2H_5)_4\overset{+}{N}Br^-$

Reaction between ethylene derivatives and N-bromosuccinimide ←
s. *9*, 606

Sulfuryl chloride SO_2Cl_2

Halogenation H → Hal
s. *9*, 584

Trihalides from ethylene derivatives ←
s. *9*, 607

Sulfuric acid *H_2SO_4*

Bromination H → Br

s. *8*, 512

p-Toluenesulfonic acid *TsOH*

s. *9*, 968

Iodine monochloride/acetic acid *ICl/CH_3COOH*

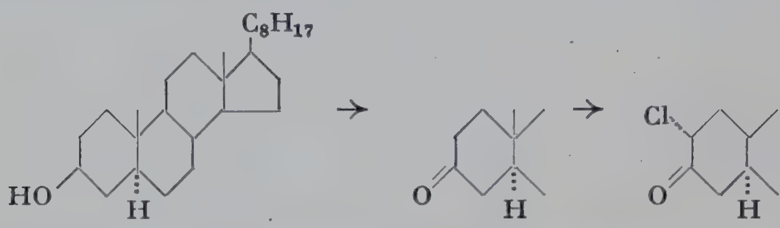
Iodination H → I

s. *2*, 493; *3*, 443; s. a. D. Papa et al., Am. Soc. *75*, 1107 (1953)

tert-Butyl hypochlorite *$(CH_3)_3C \cdot OCl$*

Ketones from sec. alcohols with subsequent chlorination CH(OH)CH → COCC

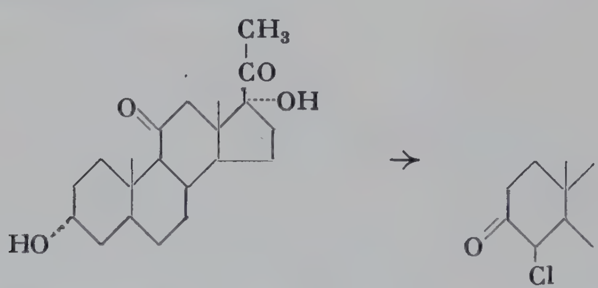
617.



t-Butyl hypochlorite in CCl_4 added dropwise to a soln. of 5.0 g. cholestan-3*β*-ol in CCl_4, and stirred 4 hrs. at room temp. → 3.82 g. cholestan-3-one dissolved in glacial acetic acid, treated at 65° with one portion of t-butyl hypochlorite, and heated 1 hr. on a steam bath → 2-chloro-cholestan-3-one (Y: 90%). Also one-step procedure and f. e. s. J. J. Beereboom et al., Am. Soc. *75*, 3500 (1953).

Oxidation-chlorination
***α*-Chloroketones from alcohols**

618.



3*α*,17*α*-Dihydroxypregnane-11,20-dione dissolved in *tert*-butanol by warming, water and HCl added at 26°, then *tert*-butyl hypochlorite added at 7-10°, and allowed to stand 6 hrs. in the dark → 4-chloro-17*α*-hydroxypregnane-3,11,20-trione. Y: 72-96.1%. F. e., also chlorination without oxidation, s. R. H. Levin et al., Am. Soc. *76*, 546 (1954); other reagents s. Am. Soc. *76*, 3179 (1954).

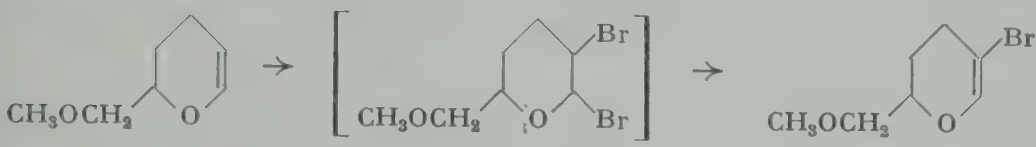
Potassium hypobromite *KOBr*

Bromoacetylenes C⋮CH → C⋮CBr

s. *4*, 494; s. a. J. D. Billimoria, Soc. *1953*, 2626

Via intermediates *v.i.*

5-Bromo-2,3-dihydropyrans H → Br

619. 

Br added at −50° to an ethereal soln. of 64 g. 2-methoxymethyl-2,3-dihydropyran, the cooling mixture removed, diethylaniline added during 5 min., and refluxed 5 hrs. → 69 g. 2-methoxymethyl-5-bromo-2,3-dihydropyran. R. Paul and S. Tchelitcheff, Bl. *1952*, 808.

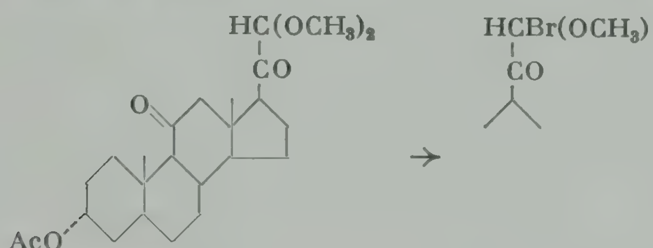
Oxygen ↑ HalC⇅O

Without additional reagents *w.a.r.*

Halides from alcohols OH → Hal

s. *9*, 108

1,1-Alkoxyhalides from acetals $C(OR)_2$ → C(OR)Hal

620. 

Dry HBr passed over the surface of a soln. of 3α-acetoxy-21,21-dimethoxypregnane-11,20-dione in chloroform at 0° for 30 min., and kept 4 additional hrs. at 0°→3α-acetoxy-21-bromo-21-methoxy-17α-pregnane-11,20-dione. Y: ca. 50%. V. R. Mattox, Am. Soc. *74*, 4340 (1952).

Acetobromosugars OAc → Br
with liquid hydrogen bromide

621. HBr condensed over β-pentaacetyl-h-galactose, and warmed 15-20 min. at room temp. in a sealed tube until dissolved → β-acetobromo-h-galactose. Crude Y: 87%. H. H. Schlubach and E. Wagenitz, H. *213*, 87 (1932); s. a. G. A. Howard, B. Lythgoe, and A. R. Todd, Soc. *1947*, 1052; F. Weygand and F. Wirth, B. *85*, 1000 (1952).

C

Dibromides from cyclic ethers

s. *8*, 607; s. a. J. Org. Chem. *19*, 1449 (1954)

Alkali halides ←

Halides from p-toluenesulfonic acid esters OTs → Hal

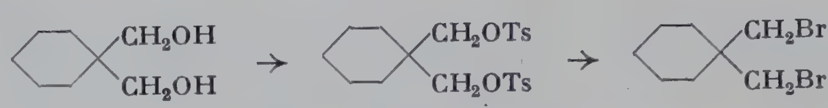
622. $$CH_3OTs + KI \rightarrow CH_3I$$

Methyl p-toluenesulfonate, KI, and water heated gradually in an oil bath with distillation → methyl iodide. Y: 94.4%.—Reaction takes place also with sulfonates of sec. hydroxyl groups. F. e. s. F. Drahowzal and D. Klamann, M. *82*, 970 (1951).

Sodium bromide *NaBr*

Replacement of hydroxyl by bromine via p-toluenesulfonic acid esters

623.



10% excess tosyl chloride added with ice-cooling and occasional swirling during 25 min. to a soln. of 368 g. 1,1-di(hydroxymethyl)cyclohexane in dry pyridine, and allowed to stand overnight at room temp. → 1,1-di(tosyloxymethyl)cyclohexane (Y: 67%; on a smaller scale, nearly 100%) heated 3 hrs. with 20% excess NaBr in diethylene glycol at 150-170° with vigorous stirring → 1,1-di(bromomethyl)cyclohexane (Y: 79%).—A one-step procedure with PBr_3 gave only 27% yield. E. R. Buchman, D. H. Deutsch, and G. I. Fujimoto, Am. Soc. *75*, 6228 (1953).

Sodium iodide *NaI*

Iodides from p-toluenesulfonic acid esters

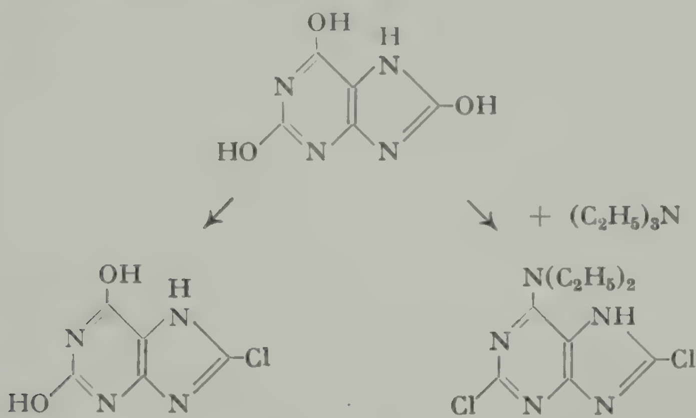
s. *2*, 121; in diethyl ketone s. S. W. Pelletier and W. A. Jacobs, Am. Soc. *74*, 4218 (1952)

624. The replacement of *sec. tosyloxy groups* in open-chain polyhydroxy compounds occurs under conditions comparable with those necessary to replace many prim. tosyloxy groups. The ease of the reaction is dependent on steric factors and is greatly diminished when the tosyl group is attached to a C-atom which is a member of a ring. E. s. N. K. Matheson and S. J. Angyal, Soc. *1952*, 1133.

Triethylamine/phosphorus oxychloride *$(C_2H_5)_3N/POCl_3$*

Replacement of hydroxyl by chlorine ←
Exchange of substituents of amines

25.



A mixture of monopotassium urate, $POCl_3$

and a limited amount of triethylamine refluxed 4.5 hrs., excess $POCl_3$ removed on a steam bath under reduced pressure, the remaining sirup poured on ice, allowed to stand 3 hrs. at room temp., refrigerated overnight to complete precipitation, and filtered → 8-chloroxanthine. Y: 85.5%.

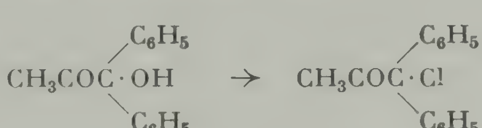
and excess triethylamine refluxed 13 hrs., excess $POCl_3$ removed under reduced pressure, the residue poured slowly with vigorous stirring on ice, kept 0.5 hr. at 0°, and filtered → 2,8-dichloro-6-diethylaminopurine. 2.1 g. from 5.0 g.

F. e. s. R. K. Robins and B. E. Christensen, Am. Soc. *74*, 3624 (1952).

Pyridine/thionyl chloride *$C_5H_5N/SOCl_2$*

Halogenoketones from hydroxyketones OH →

26.



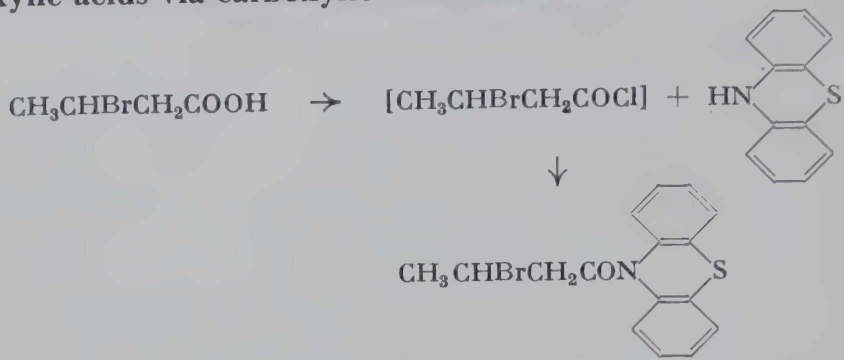
$SOCl_2$ in benzene added slowly at 0° to a soln. of α-hydroxy-α,α-diphenylacetone (prepn. s. 743) and pyridine in benzene, and warmed 3 hrs. with stirring at 50-60° → α-chloro-α,α-diphenylacetone (startg. m. f. 314). Y: 83.3%. C. L. Stevens and A. E. Sherr, J. Org. Chem. *17*, 1228 (1952).

Carboxylic acid chlorides from carboxylic acids COOH → COCl

s. *1*, 626; s. a. K. Freudenberg and H. H. Hübner, B. *85*, 1181 (1952)

Subst. carboxylic acid amides from carboxylic acids via carboxylic acid chlorides

627.



A soln. of 1 mole β-bromobutyric acid and 1 mole pyridine in anhydrous ether cautiously treated with 1 mole $SOCl_2$ in ether, kept 3 days at room temp., any excess pyridine precipitated as the hydrochloride by adding a small volume of ethereal HCl, filtered, a soln. of phenothiazine in toluene added to the filtrate, the ether evaporated, and the toluene soln. kept 4 hrs. at 85° → 10-(β-bromobutyryl)phenothiazine. Y: 81%. F. e., also amide formation at higher temp., s. R. Dahlbom and T. Ekstrand, Acta Chem. Scand. *6*, 1285 (1952).

Boron chloride *BCl_3*

Cleavage of mixed ethers ROR′ → RCl

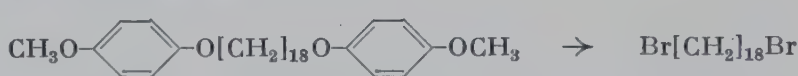
s. *9*, 194

Acetic anhydride *$(CH_3CO)_2O$*

Bromides from ethers OR → Br

Longchain α,ω-dihalides

628.

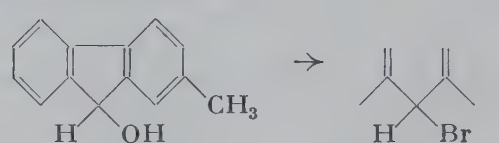


1,18-Di-p-methoxyphenoxyoctadecane refluxed 24 hrs. with a mixture of acetic anhydride and 50%-HBr (1:1) → octadecamethylene dibromide. Y: 88%. F. e. s. A. W. Nineham, Soc. *1953*, 2601.

Acetyl bromide *CH_3COBr*

Replacement of hydroxyl by bromine OH → Br

629.



A mixture of 2-methyl-9-fluorenol and acetyl bromide refluxed 10 min. → 2-methyl-9-bromofluorene. Y: 90%. F. e. s. E. D. Bergmann et al., Bl. *1952*, 78.

Acetobrominolysis of carbohydrates ←

30. Acetates of maltose or of polysaccharides having only α-1,4-glucopyranosidic linkages produce almost quantitatively acetobromoglucose.— E: Octaacetyl-β-maltose allowed to react with HBr-acetic acid-acetyl bromide for 24 hrs. → acetobromoglucose. Y: 82.5%. F. e. s. A. Jeanes, C. A. Wilham, and G. E. Hilbert, Am. Soc. *75*, 3667 (1953).

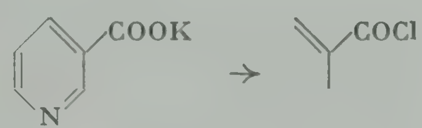
Oxalyl chloride *$(COCl)_2$*

Carboxylic acid chlorides from carboxylic acids O C

s. *9*, 474, 877

Oxalyl chloride/potassium salt *$(COCl)_2/K^+$*

31.



Oxalyl chloride in benzene added with ice-cooling to a mixture of K-nicotinate and benzene, stirring continued 15-20 min., allowed to warm to room temp., then gradually heated, and gently refluxed for 30 min. → nicotinyl chloride. Y: at least 85%.–The Na-salt did not give as good results as the K-salt. H. N. Wingfield, Jr., W. R. Harlan, and H. R. Hanmer, Am. Soc. *75*, 4364 (1953).

Phosphorus *P*

Acetobromosugars ←

s. *6*, 582; with glacial acetic acid instead of water and without $HClO_4$ s. P. G. Scheurer and F. Smith, Am. Soc. *76*, 3224 (1954)

α-Halogenocarboxylic acid halides from carboxylic acids CHCOOH → CHalCOHal

s. *9*, 876, 960

Phosphorus pentoxide/phosphoric acid/potassium iodide *$P_2O_5/H_3PO_4/KI$*

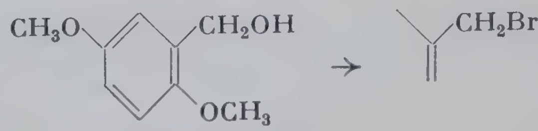
Iodides from alcohols OH → I

32. Finely powdered KI and n-octadecyl alcohol added to a cooled mixture of H_3PO_4 and P_2O_5, heated 5 hrs. at 110-120° with stirring → n-octadecyl iodide. Y: 85%. G. W. Wood, Soc. *1953*, 3327.

Phosphorus tribromide *PBr_3*

Replacement of hydroxyl by halogen OH → Hal

633.



PBr_3 in CCl_4 added slowly to an ice-cold soln. of 2,5-dimethoxybenzyl alcohol in CCl_4, and allowed to stand overnight at room temp. protected from moisture → 2,5-dimethoxybenzyl bromide. Y: 85%. A. T. Shulgin and E. M. Gal, Soc. *1953,* 1316.

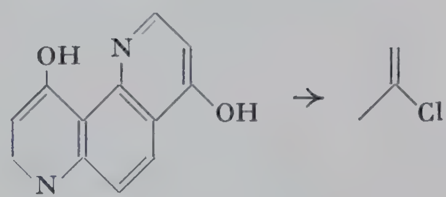
Phosphorus oxychloride/triethylamine *$POCl_3/(C_2H_5)_3N$*

s. Triethylamine/phosphorus oxychloride

Phosphorus oxychloride/phosphorus pentachloride *$POCl_3/PCl_5$*

Partial replacement of hydroxyl by chlorine OH → Cl

634.



A mixture of anhydrous 4,10-dihydroxy-1,7-phenanthroline, PCl_5, and $POCl_3$ refluxed 20 min. → 4-chloro-10-hydroxy-1,7-phenanthroline (startg. m. f. 533). Y: 77%. Also replacement of both hydroxyl groups in the absence of PCl_5 s. A. R. Surrey and R. A. Cutler, Am. Soc. *76,* 1109 (1954).

Phosphorus pentachloride *PCl_5*

1,1-Alkoxychlorides from acetals $C(OR)_2 \rightarrow CCl(OR)$

s. *2,* 731; 1,2-dialkoxy-1,2-dichloroethanes and their reactions s. H. Fiesselmann and F. Hörndler, B. *87,* 911 (1954)

Carboxylic acid chlorides from carboxylic acids COOH → COCl

s. *9,* 650

with simultaneous lactam ring closure

s. *9,* 566

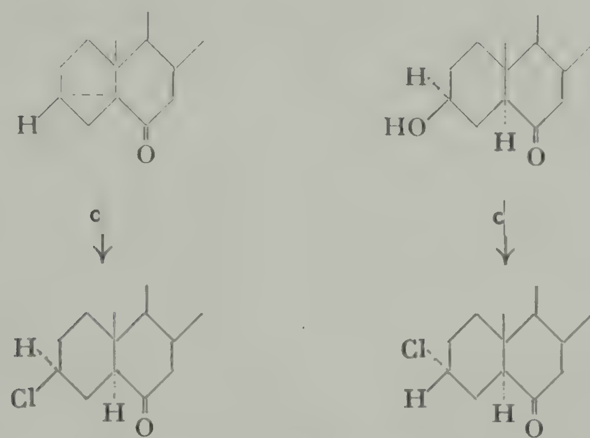
(Carbalkoxyalkylimino)chlorides from acylaminocarboxylic acid esters NHCO → N:CCl

s. *9,* 521

Phosphorus pentachloride/calcium carbonate *$PCl_5/CaCO_3$*

Halogeno- from hydroxy- and 3,5-cyclo-steroids ←
Epimerization

35.



3,5-Cyclocholestan-6-one allowed to react with HCl in acetic acid at 20° → 3β-chlorocholestan-6-one. Y: ca. 100%. (Soc. *1952*, 1786.)

PCl_5 added at 0° in small portions during 1.5 hrs. to a soln. of 4 g. 3β-hydroxycholestan-6-one in dry chloroform containing a suspension of $CaCO_3$, and shaken overnight at 20° → 4.1 g. 3α-chlorocholestan-6-one (Soc. *1952*, 1790).

F. e. s. C. W. Shoppee and G. H. R. Summers, Soc. *1952*, 1786, 1790; from 3,5-cyclosteroids s. a. Soc. *1952*, 3361.

Thionyl chloride *$SOCl_2$*

Halides from alcohols OH → Hal

s. *9*, 108

Carboxylic acid chlorides from carboxylic acids COOH → COCl

s. *9*, 503

Dicarboxylic acid chloride esters from dicarboxylic acid monoesters

36.

$$\begin{array}{c} COOCH_3 \\ | \\ CH_2 \\ | \\ CH_2 \\ | \\ COOH \end{array} \rightarrow \begin{array}{c} COOCH_3 \\ | \\ CH_2 \\ | \\ CH_2 \\ | \\ COCl \end{array}$$

Monomethyl succinate and 15% excess $SOCl_2$ allowed to stand 1 hr. at room temp. until the gas evolution subsides, warmed 3 hrs. at 37-42°,

allowed to stand overnight, then distilled → methyl ω-(chloroformyl)-propionate. Y: 85.2%. A. Kreuchunas, Am. Soc. *75*, 3339 (1953); method s. P. Ruggli and A. Maeder, Helv. *25*, 936 (1942); s. a. A. Neuberger and J. J. Scott, Soc. *1954*, 1820.

Thionyl chloride/pyridine s. Pyridine/thionyl chloride $SOCl_2/C_5H_5N$

Sulfuric acid H_2SO_4

Dibromides from cyclic ethers C

s. *9*, 597

Hydrochloric acid *HCl*

Different reactivity of halides OH → Hal

s. *9*, 570

Nitrogen ⇸ HalC ⇸ N

Fluoboric acid HBF_4

Fluorides from amines NH_2 → F
Schiemann reaction

s. *3*, 478; *4*, 509; *8*, 623; fluoroamines s. E. D. Bergmann and M. Bentov, J. Org. Chem. *19*, 1594 (1954)

Halogen ⇸ HalC ⇸ Hal

Without additional reagents *w.a.r.*

Chlorides from bromides Br → Cl

s. *5*, 413; s. a. Soc. *1953*, 2910

Aluminum chloride $AlCl_3$

Replacement of chlorine by iodine Cl → I

637. $$CH_3CHCl_2 + 2\,CH_3CH_2I \rightarrow CH_3CHI_2 + 2\,CH_3CH_2Cl$$

A mixture of 0.4 mole ethylidene chloride and 1.2 moles ethyl iodide heated 3 hrs. on a steam bath in the presence of $AlCl_3$, while ethyl chloride bubbles out of the soln. → ethylidene iodide. Y: 60%. R. L. Letsinger and C. W. Kammeyer, Am. Soc. *73*, 4476 (1951).

Sulfur ↓ HalC⇅S

Without additional reagents *w.a.r.*

Halides from disulfides RSSR → 2 RHal

638. $F_3C{\cdot}S{\cdot}S{\cdot}CF_3 \rightarrow 2\,F_3CCl$

Bis-(trifluoromethyl) disulfide and chlorine heated 5 days at 330-360° in a sealed tube → chlorotrifluoromethane. Y: 83%. G. A. R. Brandt, H. J. Emeléus, and R. N. Haszeldine, Soc. *1952*, 2198.

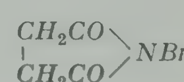
Carbon ↓ HalC⇅C

Silver salt *Ag^+*

Halides from carboxylic acids COOH → Hal
Hunsdiecker silver salt degradation

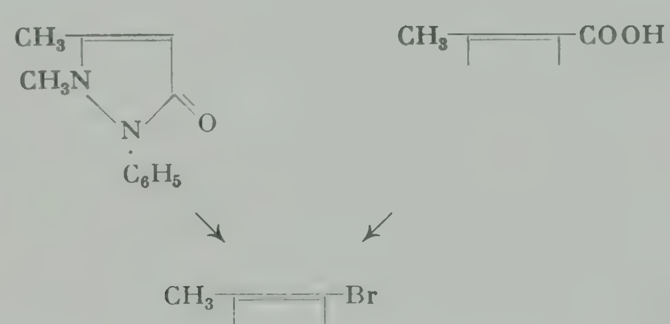
639. Portionwise addition of silver salt to the Br-soln. in CCl_4 and maintenance of low temp. are conditions favorable to the reaction. Di- and tri-bromides s. J. C. Conly, Am. Soc. *75*, 1148 (1953). Deuterium compounds s. B. Nolin and L. C. Leitch, Can. J. Chem. *31*, 153 (1953).

N-Bromosuccinimide

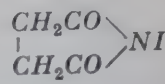


Replacement of ←
hydrogen and carbon by halogen

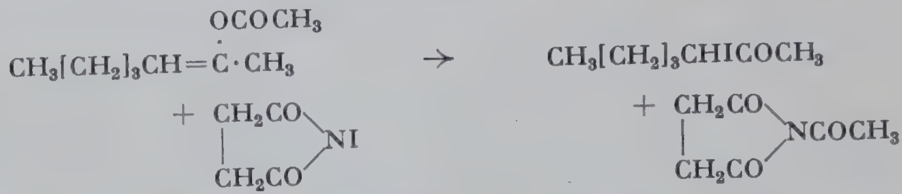
640.



Antipyrine or antipyric acid heated with N-bromosuccinimide in CCl_4, and the product isolated after 30 and 15 min. respectively → 4-bromoantipyrine. Y: 92 and 95% respectively.—F. e., also elimination of hydroxymethyl and formyl groups, s. H. de Graef, J. Ledrut, and G. Combes, Bull. soc. chim. Belges *61*, 331 (1952).

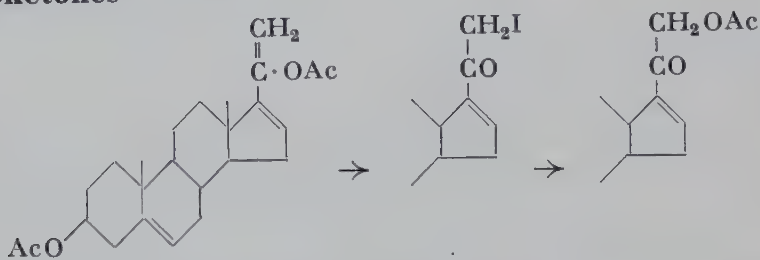
N-Iodosuccinimide 

α-Iodoöxo compounds from enolesters C:C(OAc) → ClCO

641. 

Equimolar amounts of 2-hepten-2-ol acetate and N-iodosuccinimide (prepn. s. 389) heated 15 min. at 120° → 3-iodo-2-heptanone (Y: 82%) and N-acetylsuccinimide (Y: 90%). Also α-iodoaldehyde and steroid derivative s. C. Djerassi and C. T. Lenk, Am. Soc. *75*, 3493 (1953).

α-Acoxyketones from enolesters via α-iodoketones C:C(OAc) → COC·OAc

642. 

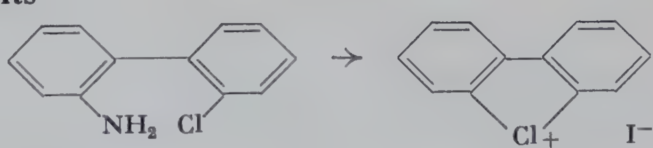
A mixture of $\Delta^{5,16,20}$-pregnatriene-3β,20-diol diacetate and N-iodosuccinimide in dioxane heated 1 hr. at 85° in a stoppered flask under N_2, methanol and a large excess of aq. KI added with stirring to the hot soln., the color then discharged by addition of Na-thiosulfate → 21-iodo-$\Delta^{5,16}$-pregnadien-3β-ol-20-one acetate (Y: 88%) dissolved in acetone, and refluxed 18 hrs. with a mixture of $KHCO_3$ and acetic acid previously ground in a mortar → $\Delta^{5,16}$-pregnadiene-3β-21-diol-20-one diacetate (Y: 90-98%). Over-all Y without purification of the intermediate: 85%. F e. s. C. Djerassi and C. T. Lenk, Am. Soc. *76*, 1722 (1954).

Elimination

Nitrogen ↑ HalC⇑N

Sodium nitrite *$NaNO_2$*

Halonium salts

643. 

1 g. 2-amino-2′-chlorobiphenyl hydrochloride in 10%-HCl treated at 0-5° with aq. $NaNO_2$, kept 30 min. at the same temp., treated with urea.

allowed to stand overnight at 5-10°, then gently heated on a steam bath until gas evolution has ceased, cooled to 5-10°, and KI added → 0.4 g. diphenylenechloronium iodide. F. e. s. R. B. Sandin and A. S. Hay, Am. Soc. *74*, 274 (1952).

Sulfur HalC ⇑ S

Without additional reagents *w.a.r.*

Halides from sulfonic acid halides $SO_2Hal \rightarrow Hal$
Thermal decomposition

644. $$(CH_3)_2CHSO_2Cl \rightarrow (CH_3)_2CHCl$$

Isopropanesulfonyl chloride distilled at an oil bath temp. of 200-220° over a period of 1.5 hrs. → isopropyl chloride. Y: 73.4%.—This method may serve to determine the position of sulfo group. F. e. s. A. P. Terent'ev and A. I. Gershenovich, Ж. *23*, 204 (1953); C. A. *48*, 2568i.

Formation of S—S Bond

Exchange

Hydrogen ↑ SS ⇅ H

Hydrochloric acid *HCl*

Disulfonyl trisulfides and thiolsulfonic acid esters from thiolsulfonic acids ←

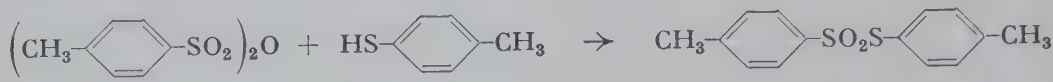
645. $$4\ p\text{-}CH_3C_6H_4SO_2SH$$
$$\downarrow$$
$$p\text{-}CH_3C_6H_4SO_2 \cdot S_3 \cdot SO_2C_6H_4CH_3\text{-}p + p\text{-}CH_3C_6H_4SO_2SC_6H_4CH_3\text{-}p + 2\,H_2O + S$$

Excess concd. HCl added at 35° in one portion to an aq. soln. of Na-p-toluenethiolsulfonate dihydrate, and the products isolated after 3 hrs. → di-p-toluenesulfonyl trisulfide (Y: 88%) and p-tolyl p-toluenethiolsulfonate (Y: 88%). F. e. s. F. Kurzer and J. R. Powell, Soc. *1952*, 3728.

Oxygen ↑ **SS⇅O**

Pyridine C_5H_5N

Thiolsulfonic acid esters from sulfonic acid anhydrides RSO_2SR'

646. 

Dry pyridine added to a soln. of p-toluenesulfonic anhydride in benzene, then p-thiocresol added during ca. 3 hrs. with stirring, and stirring continued for 3 hrs. → p-tolyl p-toluenethiolsulfonate. Y: 71%. F. e. s. L. Field, Am. Soc. *74*, 394 (1952).

Formation of S—Rem Bond

Uptake

Addition to Sulfur **SRem ⇓ SS**

Irradiation ←

Sym. di(alkylthio)mercury from sym. disulfides $RSSR \rightarrow (RS)_2Hg$

647. $$F_3C{\cdot}S{\cdot}S{\cdot}CF_3 + Hg \rightarrow (F_3C{\cdot}S)_2Hg$$

Bis(trifluoromethyl) disulfide and Hg shaken and irradiated 4 days with UV-light in a sealed silica tube → bis(trifluoromethylthio)mercury. Y: 53%. G. A. R. Brandt, H. J. Emeléus, and R. N. Haszeldine, Soc. *1952*, 2198.

Exchange

Halogen ↑ **SRem⇅Hal**

Sodium salt Na^+

Organotellurium compounds ←

648. $$3\ CH_3SO_2SNa + Cl_3TeC_6H_4OCH_3\text{-}p$$
$$\downarrow$$
$$CH_3SO_2STeC_6H_4OCH_3\text{-}p + S_2(SO_2CH_3)_2 + 3\,NaCl$$

p-Anisyl telluritrichloride and finely powdered Na-methanethiosulfonate in ethanol-free chloroform triturated for a few min., first at room temp., then at boiling temp. → p-methoxybenzenetellurenyl methanethiosulfonate. Y: 68%. O. Foss, Acta Chem. Scand. *6*, 306 (1952).

Formation of S—C Bond

Uptake

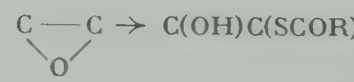
Addition to Oxygen and Carbon — SC ⇓ OC

Without additional reagents — *w.a.r.*

Sulfones from quinones — RSO_2R'

s. *2*, 542; s. a. I. S. Joffe, Ж. *23*, 125 (1953); C. A. *48*, 1299e

Hydroxythiolic acid esters from oxido compounds

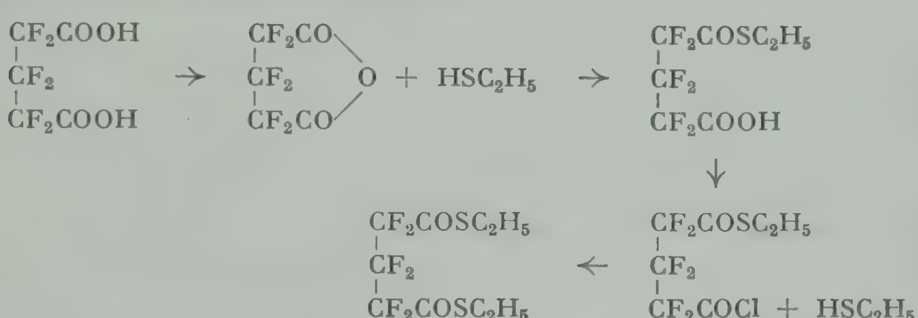


649.

Thiolacetic acid added to cyclohexene oxide, kept 60 hrs. at room temp., then distilled → *trans*-2-acetylthiocyclohexanol. Y: 84%. L. W. C. Miles and L. N. Owen, Soc. *1952*, 817.

Dithiolic acid esters from dicarboxylic acids via dicarboxylic acid anhydrides, carboxythiolic acid esters, and chlorocarbonylthiolic acid esters ←

650.



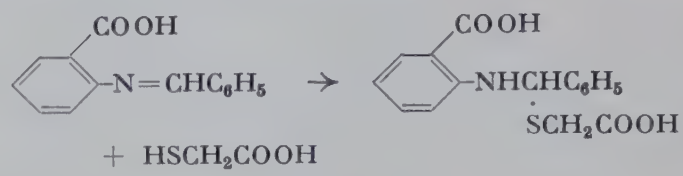
Perfluoroglutaric acid heated 8 hrs. with $POCl_3$ at 150° → perfluoroglutaric anhydride (Y: 76.5%) added to ethyl mercaptan at room temp., finally heated several hrs. at 100° → monoethyl thiolhexafluoroglutarate (Y: 95.2%) treated with excess PCl_5 → monoethyl thiolhexafluoroglutaryl chloride (Y: 83%) allowed to react with ethyl mercaptan → diethyl dithiolhexafluoroglutarate (Y: 90%).—It was necessary to employ the anhydride since the dichloride could be obtained only in low yield. M. Hauptschein, C. S. Stokes, and E. A. Nodiff, Am. Soc. *74*, 4005 (1952).

Addition to Nitrogen and Carbon SC ⇓ NC

Without additional reagents *w.a.r.*

1,1-Aminothioethers from azomethines N:C → NH·C·SR

651.



Benzalanthranilic acid and mercaptoacetic acid added to benzene, then stirred until the product precipitates (0.5-12 hrs.) → carboxymethylthiobenzylanthranilic acid. Y: 92%. F. e. s. G. W. Stacy and R. J. Morath, Am. Soc. *74*. 3885 (1952).

Acylguanylthioureas from acyldicyanodiamides ←

652.

$$C_6H_5CONH\underset{\substack{|\\ NH_2}}{C}{=}NCN + H_2S \rightarrow C_6H_5CONH\underset{\substack{\|\\ NH}}{C}\cdot NHCSNH_2$$

A slurry of benzoyldicyanodiamide in ethanol treated 9 hrs. with a slow stream of H_2S → benzoylguanylthiourea. Crude Y: 87.5%. P. Adams et al., J. Org. Chem. *17*, 1162 (1952).

n-Butylamine *n-$C_4H_9NH_2$*

Dithioöxaldiimidates from mercaptans ←

653.

$$2\ n\text{-}C_5H_{11}SH + (CN)_2 \rightarrow n\text{-}C_5H_{11}S\overset{\substack{NH\\ \|}}{C}{-}\overset{\substack{NH\\ \|}}{C}SC_5H_{11}\text{-}n$$

Cyanogen bubbled at 3° through n-amyl mercaptan containing 1 drop of n-butylamine for ca. 25 min. until the temp. decreases again after a rise to 40° → di-n-amyldithioöxaldiimidate. Y: 82%. F. e. s. H. M. Woodburn and C. E. Sroog, J. Org. Chem. *17*, 371 (1952).

Triethylamine *$(C_2H_5)_3N$*

Carboxylic acid acylthioethylamides from carboxylic acid ethylenimides ←

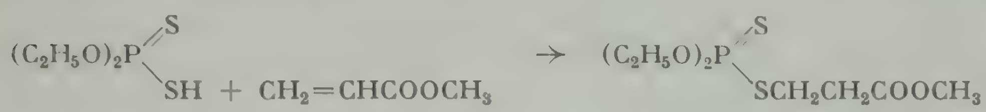
s. *9*, 454

Addition to Carbon SC ⇓ CC

Without additional reagents *w.a.r.*

Thiothionophosphoric acid esters $(RO)_2PSSR$

4.



Methyl acrylate added dropwise with stirring to O,O-diethyl thiolthionophosphoric acid at such a rate that the temp. does not rise above 100°, then heated at 100-110° with stirring until the acidity of the reaction mixture has decreased to a substantially constant value → S-carbomethoxyethyl O,O-diethyl thiolthionophosphate. Y: 83%. F. e. s. G. R. Norman, W. M. LeSuer, and T. W. Mastin, Am. Soc. *74*, 161 (1952); also abnormal addition in the presence of peroxides s. Am. Soc. *76*, 670 (1954).

Triton B ←

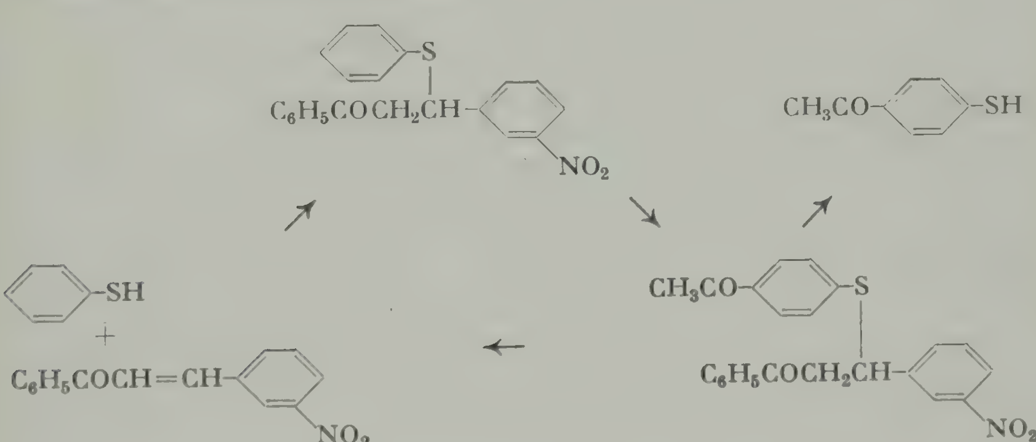
Thioethers from ethylene derivatives C:C → CHCSR

s. *4*, 540; s. a. Q. F. Soper et al., Am. Soc. *76*, 4109 (1954)

Piperidine $C_5H_{11}N$

Protection of sulfhydryl groups
by addition to ethylene derivatives
Friedel-Crafts ketone synthesis ←

55.



Thiophenol added to 3-nitrobenzalacetophenone dissolved in the minimum amount of boiling benzene, the heat source removed, piperidine dropped into the soln., then allowed to cool to room temp. → β-(3-nitrophenyl)-β-(phenylthio)propiophenone (Y: 96%) dissolved in acetyl chloride and CS_2, then added dropwise with stirring at −10° to

$AlBr_3$ in CS_2 → β-(3-nitrophenyl)-β-(4-acetylphenylthio)propiophenone (Y: 86%) dissolved in a mixture of chloroform and ethanol, stirred and treated with aq.-alc. Pb-acetate followed by enough aq. 10%-NaOH to keep the soln. at pH 8-10, the Pb-mercaptide precipitate removed by filtration (3-Nitrobenzalacetophenone can almost completely be recovered from the filtrate), and carefully triturated with dil. HCl at 0° → 4-acetylthiophenol. Over-all Y: 77%.—This is a general method for the prepn. of electrophilically subst. thiophenols. F. reactions with protection of the sulfhydryl group s. A. H. Herz and D. S. Tarbell, Am. Soc. *75*, 4657 (1953).

Borax/benzoyl peroxide *$Na_2B_4O_7/(C_6H_5COO)_2$*

Sulfonic acids from ethylene derivatives C:C → CHC·SO_3H
β-H-Perfluoroalkanesulfonic acids

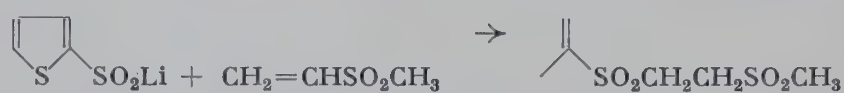
656. $CF_3CF{=}CF_2 \rightarrow CF_3CFHCF_2SO_3H$

A mixture of perfluoropropene, $NaHSO_3$, borax, water, and a little benzoyl peroxide heated 9 hrs. with agitation at 110-120° in an autoclave, the crude Na-salt mixed with 95%-H_2SO_4 and SO_3 (Sulfan β), and distilled under reduced pressure → β-H-perfluoropropanesulfonic acid. Y: 64%; conversion 93%. F. e. s. R. J. Koshar, P. W. Trott, and J. D. LaZerte, Am. Soc. *75*, 4595 (1953).

Acetic acid *CH_3COOH*

γ-Disulfones C:C → CHC·SO_2R

657.



Li-2-thiophenesulfinate refluxed in glacial acetic acid until dissolved, methyl vinyl sulfone added slowly, stirring and refluxing continued for 8 hrs. → 1-(2-thiophenesulfonyl)-2-methanesulfonylethane. Y: 46%. F. e. s. W. E. Truce and E. Wellisch, Am. Soc. *74*, 5177 (1952).

Rearrangement

Nitrogen/Carbon Type SC↶NC

Hydrochloric acid *HCl*

Aminodithiolcarbonic acid esters ←
from hydroxydithiocarbamic acid esters

s. *9*, 705

Exchange

Hydrogen ↑ SC⇅H

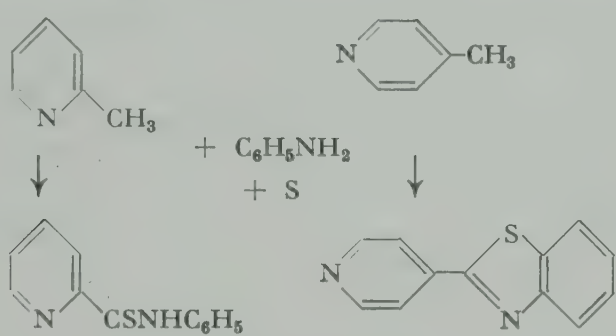
Without additional reagents *w.a.r.*

Sulfonation $H \rightarrow SO_3H$

s. *9*, 306

Extended Willgerodt reaction ←
with activated methyl and methylene groups
Carboxylic acid thioamids from hydrocarbons
Benzothiazole ring synthesis

58.



A suspension of S, aniline, and

α-picoline heated 12 hrs. in an oil bath at 160° → thiopicolinanilide. Y: 63%.	γ-picoline refluxed 24 hrs. in an oil bath at 180° → 2-(4-pyridyl)-benzothiazole. Y: 53%.

F. e. s. H. D. Porter, Am. Soc. *76*, 127 (1954).

Pyridine/sulfur trioxide C_5H_5N/SO_3

Sulfonation $H \rightarrow SO_3H$

of heterocyclics

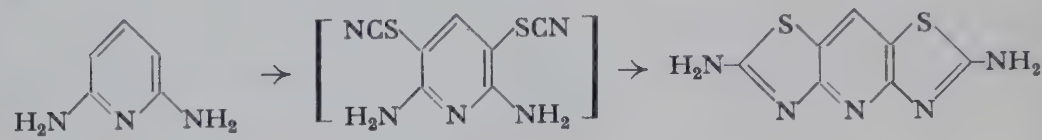
s. *3*, 508; of furans s. a. J. F. Scully and E. V. Brown, J. Org. Chem. *19*, 894 (1954)

Dioxane/sulfur trioxide ←

s. *6*, 624; s. a. A. P. Terent'ev and G. M. Kadatskii, Ж. *23*, 251 (1953); C. A. *48*, 3339b

Bromine *Br*

2-Aminothiazole ring from amines and o-aminothiocyanates Replacement of hydrogen by thiocyanato groups ←

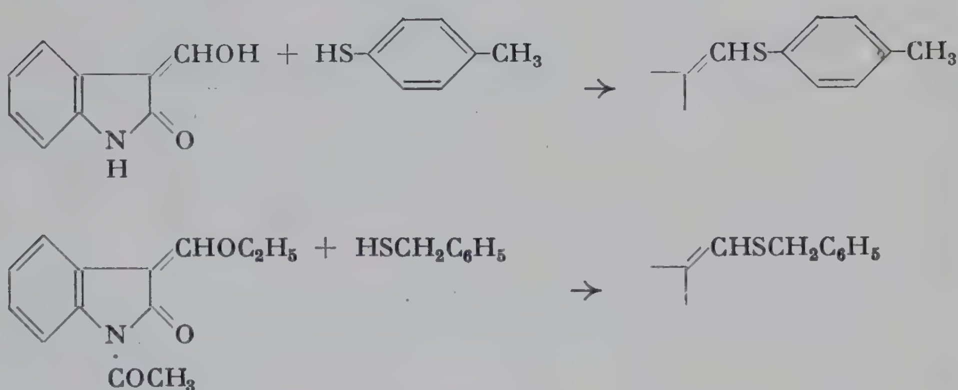
659. 

The reaction of thiocyanogen with a variety of N-heterocyclics shows that thiocyanation can readily occur if there is a sufficient number of strong "electron donating" groups present. By cyclization of o-amino-thiocyano compounds, new or otherwise difficultly accessible ring systems can be obtained.—E: Br_2 in glacial acetic acid added with stirring and ice-cooling over a period of 0.5 hr. to a soln. of 2,6-diamino-pyridine and K-thiocyanate in glacial acetic acid-methanol, the ice-bath removed, stirred 40 min., water added at 70°, and heated 15 min. at 100° → 1,7-dithia-2,6-diamino-3,4,5-triaza-s-indacene. Y: 62%. F.e.s. A. Maggiolo, Am. Soc. *73*, 5815 (1951).

Oxygen ↑ SC⇅O

Without additional reagents *w.a.r.*

Alkylthiomethylene- from hydroxymethylene- and alkoxymethylene compounds C:CHSR

660. 

3-(Hydroxymethylene)oxindole heated 1 hr. under N_2 with p-thiocresol at 120°→3-(p-tolylthiomethylene)oxindole. Y: ca. 100%.—1-Acetyl-3-(ethoxymethylene)oxindole heated similarly with benzylmercaptan at 130° → 1-acetyl-(3-benzylthiomethylene)oxindole. Crude Y: ca. 100%. F. e. s. H. Behringer and H. Weissauer, B. *85*, 774 (1952).

Reactions of hydrogen sulfide and mercaptans at high pressure ←
Reductive formation of polysulfides

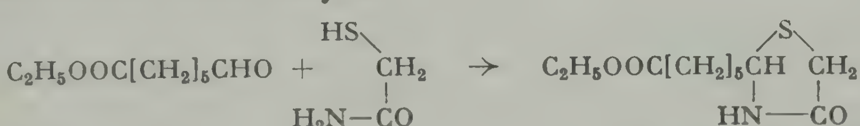
1. $2\ HCOOC_2H_5 \rightarrow (CH_3)_2S_5 + 2\ HOC_2H_5$

H_2S has greatly increased reactivity at a pressure of 8500 atm. At this pressure it can convert such compounds as methyl formate, ethyl acetate, acetamide, and cyclohexanone oxime to alkyl polysulfides. Moreover, several previously known reactions of H_2S are facilitated by such a pressure. Also, the reactivity of mercaptans is enhanced by high pressure.—E.: Ethyl formate allowed to react 14-15 hrs. with H_2S at 125° and 8500 atm. → crude methyl pentasulfide. Y: 70%. F. e. and reactions s. T. L. Cairns, A. W. Larchar, and B. C. McKusick, J. Org. Chem. *18*, 748 (1953).

Thiolic acid esters from carboxylic acid anhydrides RCOSR
s. *9*, 686

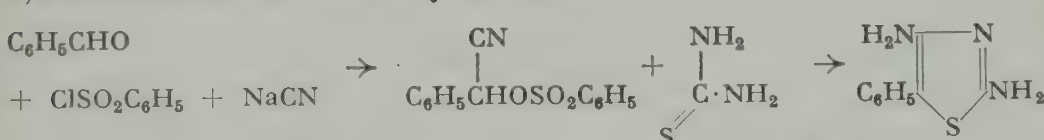
Aminomethylsulfonic acids from amines $NH_2 \rightarrow NHCH_2SO_3H$
s. *4*, 551; also with sulfonylaminomethylsulfonate groups s. K. Kraft and F. Dengel, B. *85*, 577 (1952)

4-Thiazolidones from aldehydes ○

62.


Ethyl ω-formylcaproate and thioglycolamide mixed together in xylene, and refluxed with separation of the water formed → ethyl DL-actithiazate. Y: 44%. F. e. s. R. K. Clark, Jr., and J. R. Schenk, Arch. Biochem. Biophys. *40*, 270 (1952); with p-toluenesulfonic acid s. F. C. Pennington et al., Am. Soc. *75*, 109 (1953).

2,4-Diaminothiazoles via α-cyanosulfonates

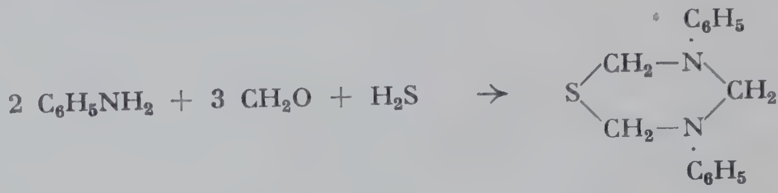
63.


A mixture of benzaldehyde, benzenesulfonyl chloride, NaCN, and water allowed to stand 3 hrs. at 0-5° with occasional shaking → α-cyanobenzyl benzenesulfonate (Y: 84%) stirred with thiourea in acetone at room temp. for 15-30 min. until soln. is achieved, and allowed to stand overnight at the same temp. → 2,4-diamino-5-phenylthiazole benzenesulfonate (Y: 80%). R. M. Dodson and H. W. Turner, Am. Soc. *73*, 4517 (1951).

←

Reaction of hydrogen sulfide with amines in the presence of formaldehyde
Tetrahydro-1,3,5-thiadiazines

664.

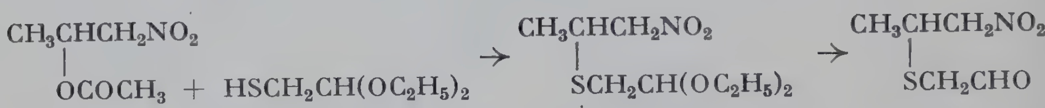


H_2S passed through a mixture of ethanol and 40%-formaldehyde until 0.5 mole has been absorbed, this soln. added at 0° to a soln. of aniline in ethanol, and kept overnight at the same temp. → 3,5-diphenyltetrahydro-1,3,5-thiadiazine. Y: 75%. F. e. and heterocyclics s. D. Collins and J. Graymore, Soc. *1953,* 4089.

Sodium/alcohol *NaOR*

Thioethers from acoxy compounds OAc → SR
Cleavage of acetals

665.

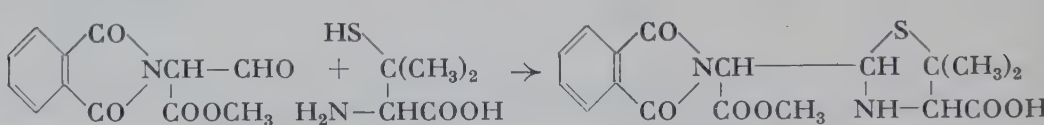


A soln. of mercaptoacetaldehyde diethylacetal in abs. ethanol added slowly at –10° to a soln. of Na in abs. ethanol, then a soln. of 2-acetoxy-1-nitropropane in ethanol added dropwise with shaking at the same temp., allowed to stand 1 hr. at –10° and 10 hrs. at 20° → 2-(1-nitropropyl) 2-(1,1-diethoxyethyl) sulfide (Y: 89%) treated with 1 *N* HCl and dioxane, then heated ca. 5 min. with vigorous stirring in a stream of CO_2 on a steam bath until dissolved → 2-(1-nitropropyl) 2-(1-oxoethyl) sulfide (Y: 95%). C. Grob und H. v. Sprecher, Helv. *35,* 902 (1952); f. e. s. *35,* 885.

Sodium acetate *CH_3COONa*

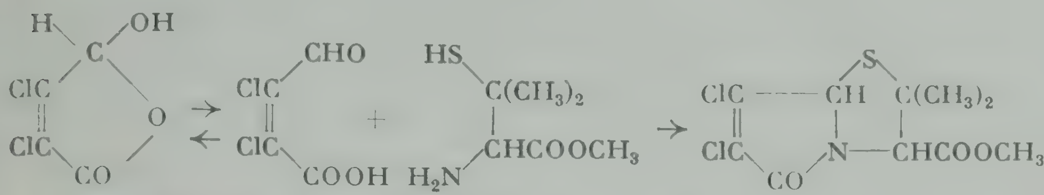
Thiazolidines

666.



An aq. soln. of DL-penicillamine hydrochloride and Na-acetate added to a hot soln. of methyl α-phthalimidomalonaldehydate in 95%-ethanol, and allowed to stand 12 hrs. at room temp. → methyl 4-carboxy-5,5-dimethyl-α-phthalimido-2-thiazolidineacetate. Y: 81%. F.e.s. J.C.Sheehan and D. A. Johnson, Am. Soc. *76,* 158 (1954).

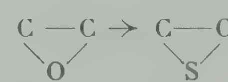
Pyrrolo[2,1-b]thiazoles

667. 

A soln. of mucochloric acid in 95%-ethanol added to a soln. containing penicillamine methyl ester hydrochloride and Na-acetate in water → 4-carbomethoxy-5,5-dimethyl-2-thiazolidine-α,β-dichloroacrylic acid γ-lactam. Y: 85%. F. e., with lower yields, s. H. H. Wasserman, F. M. Precopio, and Tien-Chuan Liu, Am. Soc. *74*, 4093 (1952).

Potassium thiocyanate *KSCN*

Ethylene sulfides from oxido compounds



s. *8*, 662; s. a. C. C. Price and P. F. Kirk, Am. Soc. *75*, 2396 (1953)

Pyridine *C_5H_5N*

Acylation of 1,1-dithiols $C(SH)_2 \rightarrow C(SAc)_2$

668.
$$(CH_3)_3C \cdot CH_2CH(CH_3)CH_2CH(SH)_2 + (CH_3CO)_2O$$
$$\downarrow$$
$$(CH_3)_3C \cdot CH_2CH(CH_3)CH_2CH(SCOCH_3)_2$$

3,5,5-Trimethyl-1,1-hexanedithiol added at 25° to acetic anhydride in pyridine, and kept 18 hrs. at the same temp. → 3,5,5-trimethyl-1,1-hexanedithiol diacetate. Y: 71%. F. e. s. T. L. Cairns et al., Am. Soc. *74*, 3982 (1952).

Pyridine/phosphorus pentasulfide *C_5H_5N/P_2S_5*

Thiolactams from lactams NHCO → NHCS

s. *9*, 574

Magnesium/ethyl alcohol *Mg/C_2H_5OH*

Sulfonylacetic acid esters from sulfonic acid anhydrides via sulfonylmalonic acid esters SO_2CH_2COOR

669.
$$C_2H_5OH + Mg + H_2C(COOC_2H_5)_2$$
$$\downarrow$$
$$(C_6H_5SO_2)_2O + C_2H_5OMgCH(COOC_2H_5)_2$$
$$\downarrow$$
$$C_6H_5SO_2CH_2COOC_2H_5 \leftarrow C_2H_5SO_2CH(COOC_2H_5)_2$$

Benzenesulfonic anhydride (prepn. s. 178) in benzene added during 1.3 hrs. to a refluxing soln. of diethyl ethoxymagnesiomalonate (pre-

pared from diethyl malonate, Mg, and ethanol in CCl_4, with subsequent addition of benzene and partial removal of solvent by distillation), and heating continued for 2 hrs. → diethyl phenylsulfonylmalonate (Y: 53%) refluxed with 25%-H_2SO_4 ca. 3 hrs. until there is no further gas evolution, then for 0.5 hr. more → ethyl phenylsulfonylacetate (Y: 82%). L. Field, Am. Soc. *74*, 394 (1952).

Boron fluoride *BF_3*

Mercaptals $C(SR)_2$

s. *8*, 667; ethylenethioketals s. a. L. F. Fieser, Am. Soc. *76*, 1945 (1954)

Trithioörthocarboxylic acid esters $C(SR)_3$

670. $$CH_3COSC_6H_5 + 2\ HSC_6H_5 \rightarrow CH_3C(SC_6H_5)_3$$

Phenyl thiolacetate, thiophenol, and BF_3 allowed to stand 14 hrs. at room temp. → phenyl trithioörthoacetate. Y: 71%. F. e., with lower yields, s. D. S. Tarbell and A. H. Herz, Am. Soc. *75*, 1668 (1953).

Aluminum chloride *$AlCl_3$*

Sulfones from sulfonic acid anhydrides RSO_2R'

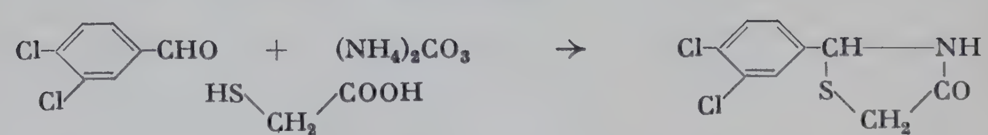
671. $$(C_6H_5SO_2)_2O + C_6H_5Br \rightarrow C_6H_5SO_2C_6H_4Br\text{-}p$$

$AlCl_3$ added with stirring at ca. 30° during 0.5 hr. to benzenesulfonic anhydride (prepn. s. 178) in bromobenzene, warmed briefly when it becomes gelatinous until it can be stirred, then stirred 1 hr. without heating and 4 hrs. at 75-85° → phenyl p-bromophenyl sulfone. Y: 74%. F. e. s. L. Field, Am. Soc. *74*, 394 (1952); *76*, 1222 (1954).

Ammonium carbonate *$(NH_4)_2CO_3$*

4-Thiazolidones from oxo compounds ○

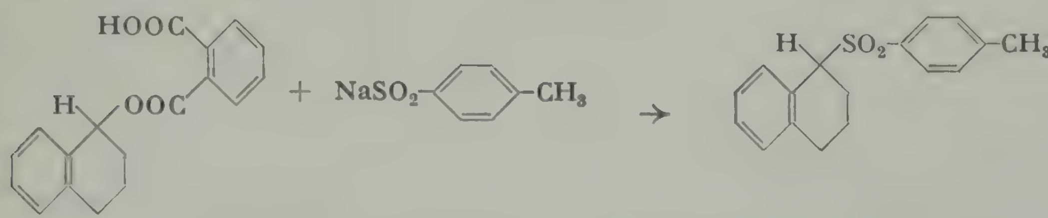
672.



A mixture of 3,4-dichlorobenzaldehyde, NH_4-carbonate, thioglycolic acid, and benzene refluxed 8 hrs. with separation of the water formed → 2-(3,4-dichlorophenyl)-4-thiazolidone. Y: 72.6%. F. e. s. A. R. Surrey and R. A. Cutler, Am. Soc. *76*, 578 (1954).

Formic or acetic acid *HCOOH or CH_3COOH*

Sulfones from sulfinic acids and alcohols RSO_2R'
Alkyl-oxygen fission

673. 

1.2,3,4-Tetrahydro-1-naphthol and its derivatives tend to react by alkyl-oxygen fission.—E: A soln. of 1,2,3,4-tetrahydro-1-naphthyl hydrogen phthalate in a little acetone added to a soln. of Na-p-toluenesulfinate in 98%-formic acid, heated 15 min. at 100°, then kept 48 hrs. at 20° → 1,2,3,4-tetrahydro-1-naphthyl p-tolyl sulfone. Y: 75%. A. G. Davies and A. M. White, Soc. *1952*, 3300; in glacial acetic acid s. M. P. Balfe, J. Kenyon, and E. M. Thain, Soc. *1952*, 790.

Lead salt *Pb^{++}*

Thiolic acid esters $RCOSR'$
from carboxylic acid anhydrides

674. $$(CH_3CO)_2O \xrightarrow{Pb(SC_6H_4CH_3\text{-}m)_2} CH_3COSC_6H_4CH_3\text{-}m$$

m-Tolyl lead mercaptide (prepared by adding excess lead acetate in 50%-alcohol to m-thiocresol) dissolved in dry pyridine, acetic anhydride added slowly, and heated 10 min. on a steam bath after the yellow color has disappeared → m-tolyl thiolacetate. Y: 80%.—The preparation from acetyl chloride gave low yields. D. S. Tarbell and A. H. Herz, Am. Soc. *75*, 1668 (1953).

Phosphorus pentasulfide *P_2S_5*

Selective replacement of oxygen by sulfur ←
in O-heterocyclics

s. *8*, 669; s. a. A. Schönberg, M. M. Sidky, and G. Aziz, Am. Soc. *76*, 5115 (1954)

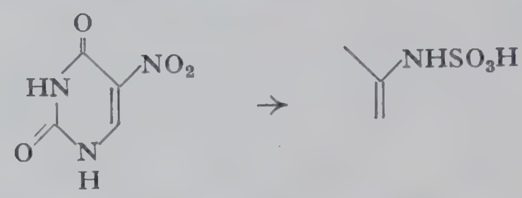
Phosphorus pentasulfide/pyridine *P_2S_5/C_5H_5N*

s. Pyridine/phosphorus pentasulfide

Hydrosulfite $S_2O_4^{--}$

Sulfamic acids from nitro compounds $NO_2 \rightarrow NHSO_3H$

675.

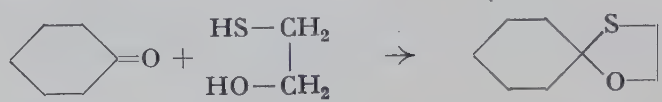


5-Nitrouracil stirred with 3 *N* NaOH, the slurry of the resulting di-Na salt treated with small portions of $Na_2S_2O_4$ alternately with NaOH in such a way that the soln. remains alkaline all the time and the $Na_2S_2O_4$ is consumed before more is added, finally the alkaline soln. containing a little unchanged $Na_2S_2O_4$ warmed to 50° and filtered → 5-sulfamino-uracil (startg. m. f. 332, 538). Y: 85-90%. F. G. Fischer, W. P. Neumann, and J. Roch, B. *85*, 752 (1952).

p-Toluenesulfonic acid *TsOH*

1,3-Oxathiolane ring ○

676.



A mixture of 2-mercaptoethanol and cyclohexanone distilled azeotropically with benzene in the presence of a little p-toluenesulfonic acid → 2-pentamethyleno-1,3-thioxolane. Y: 70%. E. D. Bergmann, D. Lavie, and S. Pinchas, Am. Soc. *73*, 5662 (1951).

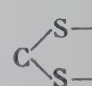
4-Thiazolidones from aldehydes
s. *9*, 662

Hydrochlorides ←

Thiazolidines
s. *2*, 543; s. a. B. E. Leach and J. H. Hunter, Biochem. Prep. *3*, 111 (1953)

Hydrochloric acid *HCl*

Mercaptals

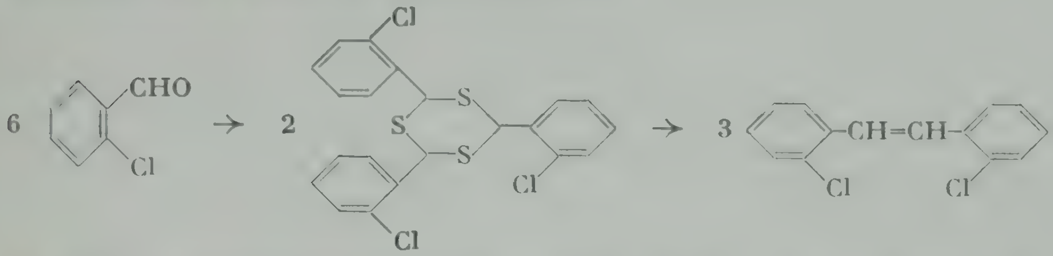


in xylene s. *6*, 643; cyclic mercaptals in dioxane s. K. Balenović, D. Cerar, and L. Filipović, J. Org. Chem. *18*, 868 (1953)

of carbohydrates
s. *1*, 469; isolation as $HgCl_2$ addition compounds s. Zaki El Heweihi, B. *86*, 781 (1953)

Stilbenes from aldehydes via s-trithianes ←

677.

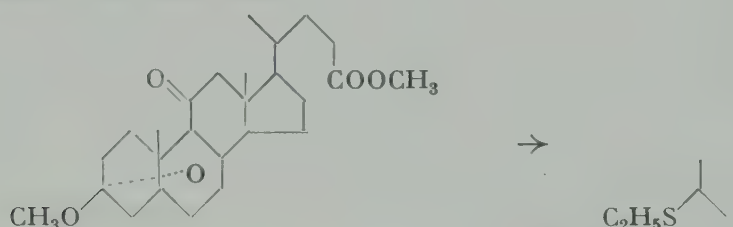


A soln. of o-chlorobenzaldehyde in ethyl acetate satd. at 2° with dry HCl, then H_2S passed in for 2 hrs. with continued introduction of HCl → α and β (*cis-cis* and *cis-trans*) o-chlorothiobenzaldehyde trimers (Y: 98.7%) and freshly prepared Cu-powder heated 1 hr. with stirring under N_2 so that the temp. is not higher than 20° above the m. p. of the startg. m. → 2,2′-dichlorostilbene (Y: 78.2%). F. e. s. J. A. Stanfield and L. B. Reynolds, Jr.. Am. Soc. *74*, 2878 (1952).

Hydrobromic acid/sodium sulfate *HBr/Na_2SO_4*

Thiolactolides from lactolides OR → SR′

678.



6 drops of 30%-HBr in acetic acid and a little Na_2SO_4 added to a soln. of methyl 3β-methoxy-3α,9α-oxido-11-ketocholanate in ethyl mercaptan, and allowed to stand 12 hrs. at room temp. → methyl 3β-ethylthio-3α.9α-oxido-11-ketocholanate. Y: 73% based on converted startg. m. H. Heymann and L. F. Fieser, Am. Soc. *73*, 5252 (1951).

Via intermediates *v.i.*

Thiolic acid esters from carboxylic acids via mixed alkoxyformic acid anhydrides COOH → COSR

s. 8, 528; s. a. R. L. Barnden et al., Soc. *1953*, 3733

Nitrogen ↑ SC⇅N

Without additional reagents *w.a.r.*

γ-Ketothioethers from tert. amines NR_2 → SR
S-β-Acylethylation

679. $C_6H_5COCH_2CH_2N(CH_3)_2 + HSCH_2C_6H_5 \rightarrow C_6H_5COCH_2CH_2SCH_2C_6H_5$

β-Dimethylaminopropiophenone and benzyl mercaptan heated 5-10 min. at 130-135° until evolution of volatile base ceases → 1,5-diphenyl-2-thiapentan-5-one. Y: 87%. F. e. s. N. S. Gill et al., Am. Soc. *74*, 4923 (1952).

Sulfonic acid amides from diazo compounds $>CN_2 \rightarrow >CHSO_2N<$

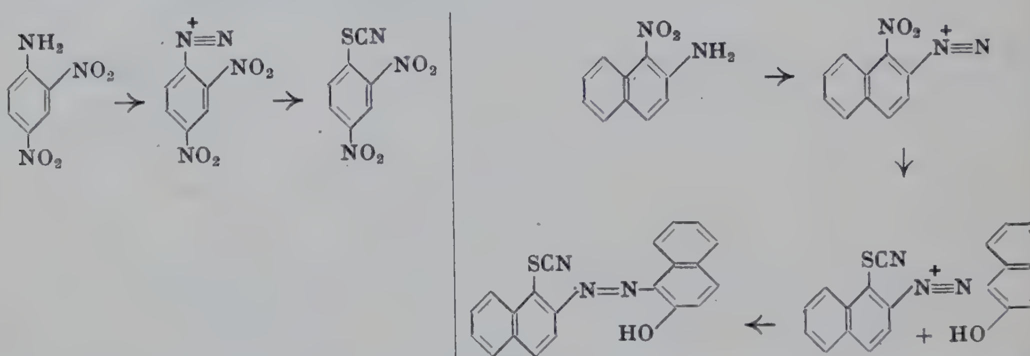
680.

Excess piperidine added to a soln. of diphenyldiazomethane in anhydrous ether, then SO_2 introduced with ice-salt cooling until the red color is discharged $\rightarrow$ diphenylmethanesulfonic acid piperidide. Y: 70%. F. e., also with NH_3, s. H. Kloosterziel, M. H. Deinema, and H. J. Backer, R. *71*, 1228 (1952).

Sodium nitrite *$NaNO_2$*

Replacement of amino by thiocyanato groups ←
Replacement of nitro by thiocyanato groups
with simultaneous formation
of azo compounds by coupling

681.



2,4-Dinitroaniline slowly added at 35° to nitrosylsulfuric acid (from $NaNO_2$ and concd. H_2SO_4), stirred 2 hrs., poured on ice, and the mixture then added to aq. K-thiocyanate $\rightarrow$ 2,4-dinitrothiocyanatobenzene. Y: almost 100%.

1-Nitro-2-naphthylamine in ethanol added to aq. H_2SO_4, quickly diazotized with $NaNO_2$ in a small amount of water, after 5 min. urea added, the diazonium soln. poured into aq. NH_4-thiocyanate, set aside for 5 min., filtered, and added to a soln. of β-naphthol, NaOH, and Na_2CO_3 in ice-water $\rightarrow$ 2-(2-hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene. Y: almost 100%.

A. Burawoy and C. Turner, Soc. *1953*, 959.

Copper *Cu*

β-Ketothioethers from α-diazoketones $COCHN_2 \rightarrow COCH_2SR$

682. $C_6H_5COCHN_2 + HSC_6H_5 \rightarrow C_6H_5COCH_2SC_6H_5$

Cu-bronze (Naturkupfer C) added at 70° to a soln. of α-diazoacetophenone and thiophenol in abs. ethanol until no further gas evolution occurs, then stirred 7 hrs. at 70-75° $\rightarrow$ α-phenylmercaptoacetophenone. Y: 67%. P. Yates, Am. Soc. *74*, 5376 (1952).

Thioacetamide *CH_3CSNH_2*

Sym. thioethers from tert. amines $2\ RNR'_2 \rightarrow R_2S$

683.

$$2\ C_6H_5COCH_2CH_2N(CH_3)_2 + CH_3C\begin{matrix}\nearrow S \\ \searrow NH_2\end{matrix}$$

$$\downarrow$$

$$(C_6H_5COCH_2CH_2)_2S + CH_3C{\equiv}N + 2\,(CH_3)_2NH$$

A mixture of β-dimethylaminopropiophenone and thioacetamide heated 15 min. at 140-145° → 1,7-diphenyl-4-thiaheptane-1,7-dione. Y: 62%. N. S. Gill et al., Am. Soc. *74*, 4923 (1952).

Ammonium chloride *NH_4Cl*

Thioethers from amines ←

s. *9*, 411

Via intermediates *v.i.*

Mercaptans from amines $NH_2 \rightarrow SH$

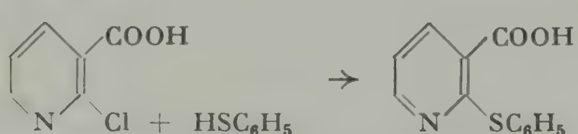
s. *3*, 517; s. a. D. Greenwood and H. A. Stevenson, Soc. *1953*, 1514

Halogen ↓ SC⇅Hal

Without additional reagents *w.a.r.*

Thioethers from halides Hal → SR

684.



A mixture of 1.57 g. 2-chloronicotinic acid and 2 cc. thiophenol heated at 140° until a clear soln. results, then 1 hr. at 185-190° → 1.58 g. 2-(3-carboxypyridyl) phenyl sulfide.—Considerable decomposition occurs, when the Na-derivative of thiophenol is used; apparently, an acid media is necessary for the reaction. F. e. s. F. G. Mann and J. A. Reid, Soc. *1952*, 2057.

Sym. disulfides from halides $2\ RHal \rightarrow RSSR$

685. $$2\ F\ CI + 2\ S \rightarrow F_3C{\cdot}S{\cdot}S{\cdot}CF_3$$

Trifluoroiodomethane and sulfur in an autoclave filled with N_2 to atmospheric pressure, and heated 30 hrs. at 220° and 24 hrs. at 265° → bis(trifluoromethyl) disulfide. Y: 60%. G. A. R. Brandt, H. J. Emeléus, and R. N. Haszeldine, Soc. *1952*, 2198.

Thiolic acid esters
from carboxylic acid chlorides COCl → COSR

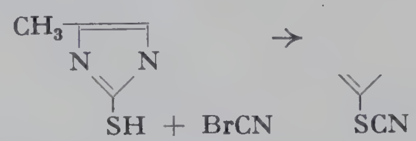
s. *9*, 650

686. $$C_3F_7COCl + HSC_2H_5 \rightarrow C_3F_7COSC_2H_5$$
$$(CF_3CO)_2O + HSC_2H_5 \rightarrow CF_3COSC_2H_5$$

and carboxylic acid anhydrides. Ethyl mercaptan treated at room temp. with 20-30% excess n-heptafluorobutyryl chloride, then heated several hrs. at 100° to complete the reaction → ethyl n-thiolheptafluorobutyrate. Y: 90%.—Similarly with trifluoroacetic anhydride → ethyl thioltrifluoroacetate. Y: 84%. F.e.s. M. Hauptschein, C. S. Stokes, and E. A. Nodiff, Am. Soc. *74*, 4005 (1952); aminothiolic acid esters from carboxylic acid chlorides s. M. Kopp and B. Tchoubar, Bl. *1952*, 84.

Thiocyanates from mercaptans SH → SCN

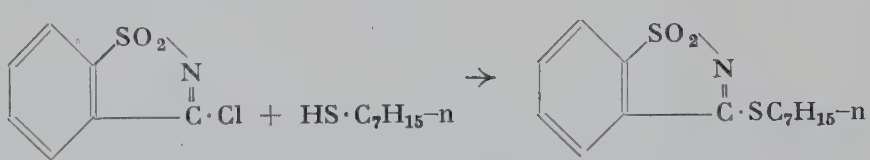
687.



Cyanogen bromide and 4(5)-methyl-2-mercaptoimidazole thoroughly mixed, then warmed 0.5-1 hr. at 45-55° → 4(5)-methyl-2-thiocyanoimidazole. Y: 59%. F. e. s. R. E. Koeppe and J. L. Wood, Am. Soc. *75*, 4655 (1953).

Identification of mercaptans
as saccharin derivatives ←

688.



Saccharin chloride and a slight excess n-heptyl mercaptan warmed 10 min. on a steam bath until the HCl-evolution ceases → S-n-heptylthiosaccharin. Y: 70%. F. e. s. J. R. Meadow and J. C. Cavagnol, J. Org. Chem. *17*, 488 (1952).

S-Alkylation of thiourea derivatives ←

of thiosemicarbazones s. *9*, 554; of other thiourea derivatives s. E. S. Scott and L. F. Audrieth, J. Org. Chem. *19*, 1231 (1954)

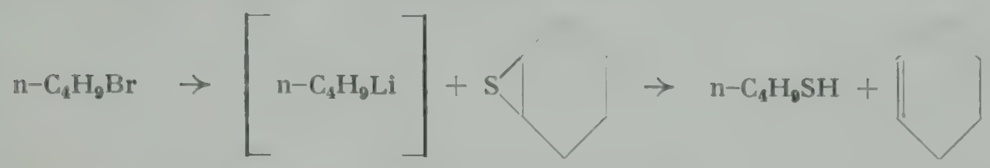
Isothiouronium salts ←

s. *9*, 589

Lithium *Li*

Mercaptans from halides ←
Ethylene derivatives from ethylenesulfides

689.

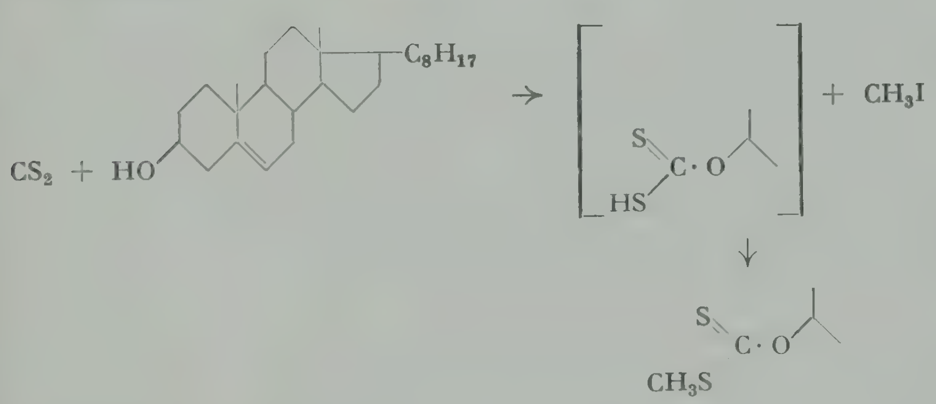


An ethereal soln. of cyclohexene sulfide added during 0.5 hr. with gentle refluxing to a soln. of n-butyl-Li, prepared from n-butyl bromide and Li in ether, stirring continued for 2 hrs., allowed to stand overnight, then poured on ice-water → 1-butanethiol (Y: 63%) and cyclohexene (Y: 67%).
The reaction of aryllithium reagents and the readily available propylene sulfide constitutes a new method for preparing thiophenols. It serves as an alternative to the reaction of aryl Grignard reagents and sulfur (S_8), which is awkward due to the insolubility of sulfur in ether, and usually gives very poor yields.—E: Phenyl-Li from bromobenzene and propylene sulfide → thiophenol. Y: 81%. F. e. s. F. G. Bordwell, H. M. Andersen, and B. M. Pitt, Am. Soc. *76*, 1082 (1954).

Sodium hydride *NaH*

Xanthates and trithiocarbonic acid esters from halides ←

690.



A mixture of cholesterol and NaH in dry benzene refluxed 24 hrs. with stirring, with addition of a trace of ethanol to start the reaction if no H_2-evolution takes place, allowed to cool to room temp., dry CS_2 added, refluxed again 24 hrs. with stirring, cooled to room temp., methyl iodide added, stirring and refluxing continued for 24 hrs. → cholesteryl-S-methyl xanthate Y: 85%. F. e. s. G. L. O'Connor and H. R. Nace, Am. Soc. *74*, 5454 (1952); also trithiocarbonic acid esters from mercaptans s. Am. Soc. *75*, 2118 (1953).

Potassium hydroxide *KOH*

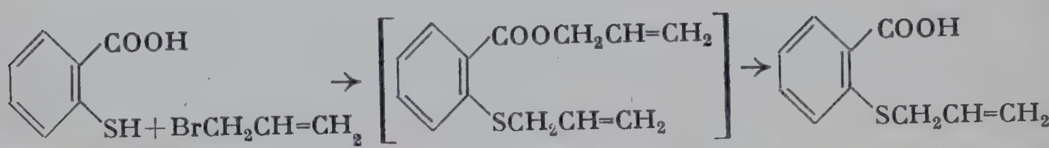
Carboxythioethers from halogenonitriles ←

691. $n\text{-}C_4H_9SH + ClCH_2CH_2CH_2CN \rightarrow n\text{-}C_4H_9SCH_2CH_2CH_2COOH$

0.5 mole aq. KOH, 0.3 mole 1-butanethiol, and 0.3 mole γ-chlorobutyronitrile added consecutively to alcohol, refluxed 1.5 hrs., more aq. KOH added, and refluxing continued for 3 hrs. → γ-(butylmercapto)butyric acid. Y: 76%. F. G. Bordwell, H. M. Andersen, and B. M. Pitt, Am. Soc. *76*, 1082 (1954).

Potassium carbonate *K_2CO_3*

Carboxythioethers ←

692. 

Allyl bromide added dropwise to a vigorously stirred suspension of K_2CO_3 and thiosalicylic acid in methyl ethyl ketone and acetone, stirring continued 3 hrs. during which reflux temp. is gradually reached, more allyl bromide and water added, refluxing continued for 15 hrs., concentrated under reduced pressure, 15%-NaOH soln. added, and refluxed 1 hr. → crude S-allylthiosalicylic acid. Y: 93%. D. S. Tarbell and M. A. McCall, Am. Soc. *74*, 48 (1952).

Potassium thiocyanate *KSCN*

Thiocyanates from halides Hal → SCN

s. *3*, 566; s. a. A. H. Schlesinger and D. T. Mowry, Am. Soc. *76*, 585 (1954); from bromides s. 4, 566; from chlorides s. A. P. Terent'ev and A. I. Gershenovich, Ж. *23*, 204 (1953); C. A. *48*, 2568i

Sodium sulfide *Na_2S*

Cyclic thioethers ○

s. *1*, 484; s. a. S. F. Birch, R. A. Dean, and E. V. Whitehead, J. Org. Chem. *19*, 1449 (1954)

Potassium hydrogen sulfide *KHS*

Mercaptans from halides Hal → SH

s. *3*, 522; s. a. H. Zinner, B. *86*, 825 (1953)

Sodium sulfite *Na_2SO_3*

Reactions with iodonium salts ←
Sulfonic acids from iodonium salts

693. $(C_6H_5)_2I^+\ Br^- + Na_2SO_3 \rightarrow C_6H_5SO_3Na + C_6H_5I + NaBr$

A mixture of diphenyliodonium bromide, Na-sulfite, and water refluxed 1 hr. → Na-benzenesulfonate. Y: 95%. F. e. and reactions s. F. M. Beringer et al., Am. Soc. *75*, 2708 (1953).

Sodium salt *Na^+*

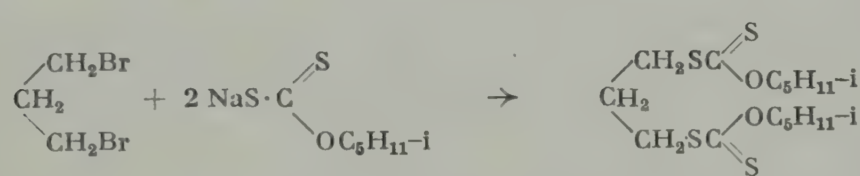
Alkylthiomethylsilanes Hal → SR

694. $n\text{-}C_4H_9SNa + BrCH_2Si(CH_3)_3 \rightarrow n\text{-}C_4H_9SCH_2Si(CH_3)_3$

Bromomethyltrimethylsilane added dropwise with stirring during 15 min. to a soln. of Na-n-butylmercaptide in abs. ethanol, then refluxed 2 hrs. → trimethylsilylmethyl n-butyl sulfide. Y: 92.5%. F. e. s. D. C. Noller and H. W. Post, J. Org. Chem. *17*, 1393 (1952).

Xanthates from halides Hal → SCS(OR)

695.



1,3-Dibromopropane allowed to react with Na-isoamylxanthate in acetone at 20° 1 hr. → crude trimethylenebis(isoamylxanthate). Y: 90%. F. e. s. D. Lefort and G. Hugel, Bl. *1952*, 172.

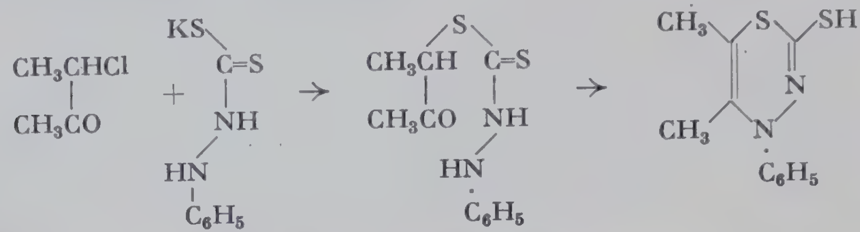
Bis(triarylthiomethyl) trisulfides ←

696. $\left.\begin{matrix} Cl_3CSCl \\ C_6H_5SNa \end{matrix}\right\rangle \rightarrow (C_6H_5S)_3CSSSC(SC_6H_5)_3$

An ethereal soln. of trichloromethylsulfenyl chloride added at −12° to an alc. soln. of Na-phenylmercaptide (prepared from phenylmercaptan and Na-ethoxide) → bis(triphenylthiomethyl) trisulfide. Y: 66.5%. F. e. s. H. J. Backer and E. Westerhuis, R. *71*, 1071 (1952); f. method s. R. *71*, 1082.

Potassium and ammonium salts *K^+ and NH_4^+*

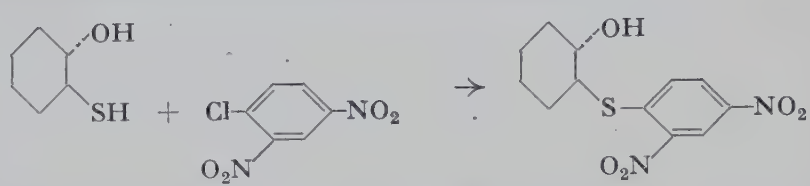
1,3,4-Thiadiazines via
α-(dithiocarbazyl)oxo compounds

697.


A 20% aq. soln. of K-phenyldithiocarbazate added at 5-9° during 30 min. to a well-stirred mixture of 3-chloro-2-butanone and 50%-ethanol → crude 3-(2-phenyldithiocarbazyl)-2-butanone (Y: 92%) added to HCl, and heated to 70° with stirring → 5,6-dimethyl-2-mercapto-4-phenyl-1,3,4,4H-thiadiazine (Y: 86%). F. e., also one-step procedure and with NH_4-salts, s. R. A. Mathes, J. Org. Chem. *17*, 877 (1952).

Pyridine *C_5H_5N*

Hydroxythioethers from hydroxymercaptans SH → SR

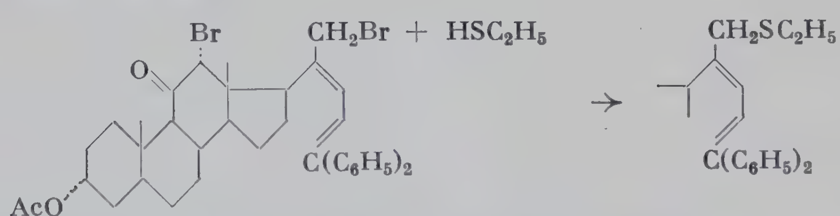
698.


A mixture of *trans*-2-hydroxycyclohexanethiol and 1 mole 2,4-dinitrochlorobenzene dissolved in pyridine heated 1 hr. on a steam bath → 2,4-dinitrophenyl *trans*-2-hydroxycyclohexyl sulfide. Y: 87%. F. e. s. F. G. Bordwell and H. M. Andersen, Am. Soc. *75*, 4959 (1953).

Thiolic acids from carboxylic acid chlorides COCl → COSH
s. *1*, 491; s. a. C. S. Marvel and E. A. Kraiman, J. Org. Chem. *18*, 707 (1953)

Calcium carbonate *$CaCO_3$*

Thioethers from halides Hal → SR

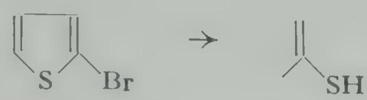
699.


A mixture of 4 g. 3α-acetoxy-11-keto-12,21-dibromo-24,24-diphenyl-$\Delta^{20,22;23}$-choladiene (prepn. s. 927), $CaCO_3$, and ethyl mercaptan shaken 16 hrs. at room temp. → 3.9 g. crude 3α-acetoxy-11-keto-12-bromo-21-

thioethyl-24,24-diphenyl-$\Delta^{20,22;23}$-choladiene. J. Heer and A. Wettstein, Helv. *36*, 891 (1953).

Magnesium *Mg*

Mercaptans from bromides Br → SH

700. 

Powdered S added to ethereal 2-thienyl-MgBr (prepared from 2-thienyl bromide and Mg-turnings in the presence of a crystal of iodine) at a rate to maintain gentle refluxing, which is continued for 1 hr. after the addition → crude 2-thiophenethiol. Y: 67%. W. H. Houff and R. D. Schuetz, Am. Soc. *75*, 6316 (1953).

Zinc chloride/sodium sulfate *$ZnCl_2/NaSO_4$*

Mercaptals $C\begin{smallmatrix}\diagup S- \\ \diagdown S-\end{smallmatrix}$

s. *7*, 116; cyclic mercaptals s. C. R. Engel and G. Just, Am. Soc. *76*, 4909 (1954)

Via intermediates *v.i.*

Replacement of hydrogen by sulfhydryl via oxazolones H → SH

s. *5*, 450; s. a. B. E. Leach and J. H. Hunter, Biochem. Prep. *3*, 111 (1953)

Sulfur ↓ SC⇅S

Without additional reagents *w.a.r.*

S-Acylation SH → SAc

701. $$R\cdot SH + HSCOCH_3 \rightarrow R\cdot SCOCH_3$$

$$HOCH_2C(CH_3)_2CH(OH)CONHCH_2CH_2CONHCH_2CH_2=R$$

Thiolacetic acid added to aq. pantetheine, and the mixture stirred overnight at room temp. → S-acetylpantetheine. Y: ca. 100%. E. Walton et al., Am. Soc. *76*, 1146 (1954).

Sodium/alcohol *NaOR*

Replacement of hydrogen by alkylthio groups H → SR

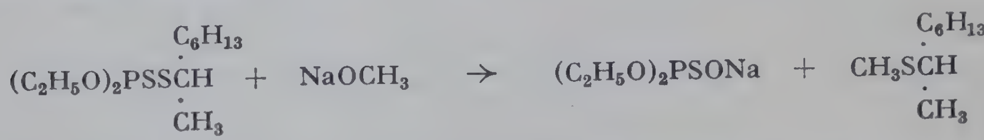
s. *5*, 453; s. a. Bl. Soc. chim. Belg. *62*, 3 (1953)

Remaining Elements ↓ SC⇅Rem

Sodium/alcohol *NaOR*

Thioethers from thiolthionophosphoric acid esters and alcohols ←

702.



O,O-Diethyl S-(2-octyl) phosphorodithioate added dropwise during 20 min. to a refluxing soln. of Na in abs. methanol, then refluxed 6 hrs., cooled to 30°, and blown with CO_2 for 1 hr. → methyl 2-octyl sulfide (Y: 65%) and Na-O,O-diethyl phosphorothioate (Y: 63%). F. e. s. W. E. Bacon and W. M. LeSuer, Am. Soc. *76*, 670 (1954).

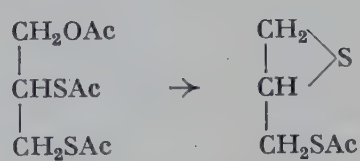
Elimination

Oxygen ↓ SC⇑O

Sodium hydrogen carbonate *$NaHCO_3$*

Cyclic thioethers by deacylation ○

703.

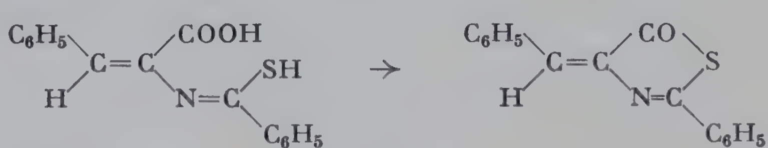


2,3-Bis(thioacetyl)propyl 1-acetate added to a warm aq. $NaHCO_3$-soln., then steam-distilled at 60°/150 mm for 3 hrs. → 3-acetylthiopropylene sulfide. Y: 80%. F. e. from partially acetylated hydroxymercaptans, s. L. W. C. Miles and L. N. Owen, Soc. *1952*, 817.

Acetic anhydride *$(CH_3CO)_2O$*

5-Thiazolones

704.

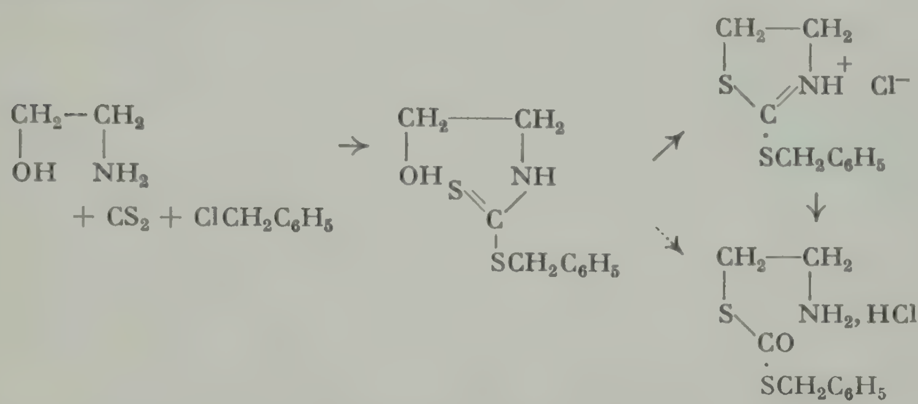


α-(Thiobenzamido)cinnamic acid heated 20 min. with acetic anhydride → 2-phenyl-4-benzylidene-5(4H)-thiazolone. Y: 85%. S. I. Lur'e and L. G. Gatsenko, Ж. *22*, 262 (1952); C. A. *47*, 2168c.

Thionyl chloride or hydrochloric acid *$SOCl_2$ or HCl*

Aminodithiolcarbonic acid esters via hydroxydithiocarbamic acid esters and thiazolines

705.



Triethylamine and CS_2 added with water-cooling to ethanolamine in pyridine, cooled to 0°, kept 1 hr. at this temp., benzyl chloride added, and the soln. kept at 0° overnight → 2-N-dithiocarbobenzyloxyamino-ethanol (Y: 90%) treated with cold $SOCl_2$ or HCl → 2-benzylthio-Δ^2-thiazoline hydrochloride (Y: 82%), 12 g. refluxed 4 hrs. with 6 *N* HCl → 11.35 g. 2-aminoethyl benzyl dithiolcarbonate hydrochloride (startg. m. f. 577). F. e., also without isolation of the thiazoline, s. J. C. Crawhall and D. F. Elliott, Soc. *1952*, 3094.

Hydrochloric acid *HCl*

Thioöxindoles from o-mercaptophenylacetic acids

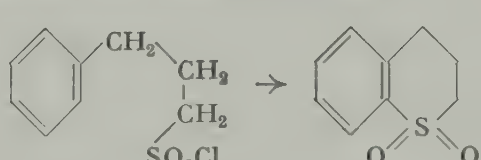
s. *9*, 121

Halogen ↑ SC ⇑ Hal

Aluminum chloride *$AlCl_3$*

Cyclic sulfones from sulfonic acid chlorides ○

706.



A soln. of 3-phenyl-1-propanesulfonyl chloride in nitrobenzene added with stirring to a cold soln. of $AlCl_3$ in the same solvent, the ice bath removed, and the reaction allowed to proceed at 87-90° for 2.5 hrs. →

thiachroman 1,1-dioxide. Y: 76.2%. F. e., with lower yields, s. W. E. Truce et al., Am. Soc. *74*, 974 (1952); *75*, 3359 (1953).

Carbon ↓ **SC ⇑ C**

Sodium hydroxide *NaOH*

1,2-Dihydro-1-keto-2-thianaphthalenes from rhodanines ←

s. *8*, 693; s. a. Soc. *1952*, 4397

Formation of Rem—Rem Bond

Exchange

Halogen ↓ **RemRem ⇅ Hal**

Sodium, potassium *Na,K*

Disilanes from halogenosilanes $>$Si · Si$<$

s. *8*, 695; with Na and a trace of K s. R. A. Benkeser and D. J. Foster, Am. Soc. *74*, 5314 (1952)

Mercury *Hg*

Biarsines $>$As · As$<$

707. $$2\ (F_3C)_2AsI \rightarrow (F_3C)_2As \cdot As(CF_3)_2$$

Iodobis(trifluoromethyl)arsine gently shaken with Hg in a sealed tube, and the product isolated after 2 days at room temp. → tetrakis(trifluoromethyl)biarsine. Y: 91%. G. R. A. Brandt, H. J. Emeléus, and R. N. Haszeldine, Soc. *1952*, 2552 (1952).

Remaining Elements ↓ **RemRem ⇅ Rem**

Sodium, potassium *Na,K*

Disilanes by interchange $>$Si · Si$<$

s. *8*, 695; s. a. Am. Soc. *76*, 278 (1954)

Formation of Rem — C Bond

Uptake

Addition to Oxygen and Carbon **RemC ⇓ OC**

Without additional reagents *w.a.r.*

α-Hydroxyphosphonic acid esters from oxo compounds $CO \rightarrow C(OH)PO(OR)_2$

708.

$$C_6H_5CHO + BrMgPO(OC_2H_5)_2 \rightarrow C_6H_5CH\begin{matrix} \diagup OH \\ \diagdown PO(OC_2H_5)_2 \end{matrix}$$

Benzaldehyde in anhydrous ether added to the bromomagnesium derivative of diethyl phosphite, and refluxed 3 hrs. $\rightarrow$ crude diethyl α-hydroxybenzylphosphonate. Y: 61.5%. F. e. s. O. Gawron et al., Am. Soc. *75*, 3591 (1953).

Sodium/alcohol *NaOR*

1-Hydroxy-2-ethylenephosphonic acid esters from α,β-ethylenealdehydes

s. *9*, 710

Addition to Carbon **RemC ⇓ CC**

Without additional reagents *w.a.r.*

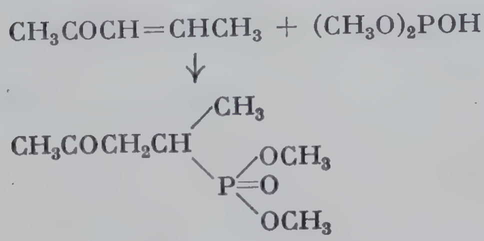
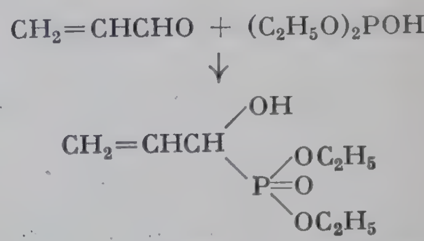
Cyanoethylation of phosphines $PH \rightarrow PCH_2CH_2CN$

709. $(C_6H_5)_2PH + CH_2{=}CHCN \rightarrow (C_6H_5)_2PCH_2CH_2CN$

Diphenylphosphine (prepn. s. 57) and acrylonitrile added in turn to a glass tube cooled in Dry Ice and filled with N_2, the tube sealed, and heated 7 hrs. at 130° $\rightarrow$ 2-cyanoethyldiphenylphosphine. Y: 71%.—The reaction proceeds readily without a catalyst, whereas that with aniline and with diphenylamine is vigorously promoted by an acidic catalyst, and that with phenylarsine by a basic catalyst. F. e. s. F. G. Mann and I. T. Millar, Soc. *1952*, 4453.

Sodium/alcohol *NaOR*

Reactions with dialkyl phosphites ←
3-Ketophosphonic acid esters
from α,β-ethyleneketones
1-Hydroxy-2-ethylenephosphonic acid esters
from α,β-ethylenealdehydes

710.  

A soln. of Na-methoxide in methanol added dropwise to a mixture of dimethyl phosphite and 3-penten-2-one at such a rate as to keep the temp. at 60-70° → 4-(dimethylphosphono)-2-pentanone. Y: 69%. (Ж. *22*, 462.)

A soln. of Na-ethoxide in ethanol added dropwise to a mixture of diethyl phosphite and acrolein → diethyl 1-hydroxy-2-propene-1-phosphonate. Y: 77% (Ж. *22*, 467.)

F. e. s. A. N. Pudovik and Y. P. Kitaev, Ж. *22*, 462, 467 (1952); C. A. *47*, 2686f/7a.

Rearrangement

Oxygen/Carbon Type RemC↶OC

Ethyl iodide *C_2H_5I*

Phosphonic acid esters from phosphites ←

s. *8*, 696; with ethyl tosylate instead of ethyl iodide s. T. C. Myers, S. Preis, and E. V. Jensen, Am. Soc. *76*, 4172 (1954)

Exchange

Hydrogen ↑ RemC⇅H

Without additional reagents *w.a.r.*

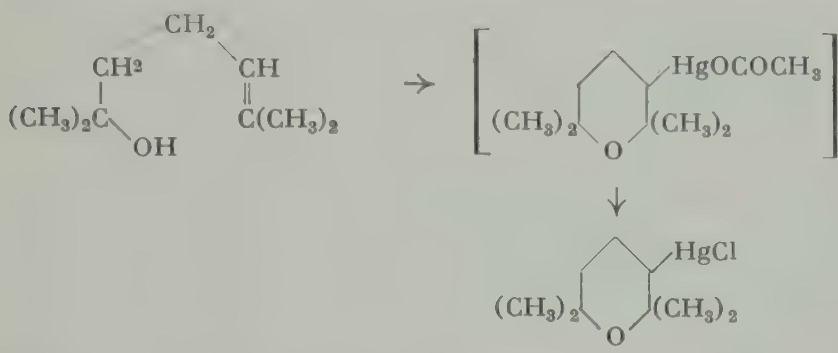
Phosphonyl dichlorides from alcohols $OH \rightarrow POCl_2$

711. $(p\text{-}CH_3C_6H_4)_3C\cdot OH + PCl_3 \rightarrow (p\text{-}CH_3C_6H_4)_3C\cdot POCl_2$

Finely powdered tri-p-tolylcarbinol added at 0° during 0.5 hr. in small portions with frequent shaking to PCl_3, allowed to reach room temp., then heated 4-5 hrs. at 60-70° → tri-p-tolylmethylphosphonyl dichloride. Y: 75%. F. e. and hydrolysis s. D. V. N. Hardy and H. H. Hatt, Soc. *1952*, 3778.

Mercurypyrans
Chloro- from aceto-mercury compounds

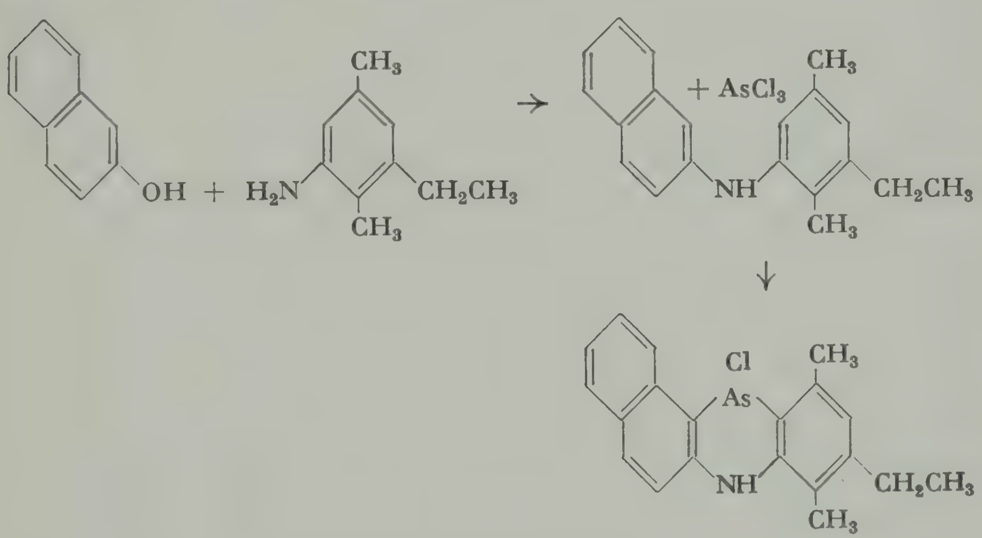
712.



A suspension of mercuric acetate in 2,6-dimethyl-2-hepten-6-ol vigorously shaken for 3 hrs., excess dimethylheptenol distilled molecularly at 35-50°/10^{-3} mm, the residue dissolved in aq. 10%-NaOH, treated with satd. NaCl, then with excess CO_2-gas → 2,2,6,6-tetramethyl-3-chloromercuritetrahydropyran. Y: 91%.—Reaction with mercuric acetate in water gives a lower yield. A. G. Brook, A. Rodgman, and G. F. Wright, J. Org. Chem. *17*, 988 (1952).

Phenarsazine ring
Sec. from prim. amines and phenols

713.



A mixture of 3 g. 3-ethyl-2,5-dimethylaniline, 7.5 g. β-naphthol, and a little iodine heated 12 hrs. at 190-200° → 4 g. N-(3-ethyl-2,5-dimethylphenyl)-β-naphthylamine, 2 g. refluxed 1 hr. with $AsCl_3$ in o-dichlorobenzene → 1.8 g. 12-chloro-9-ethyl-8,11-dimethyl-7,12-dihydrobenzo[*a*]phenarsazine. Ng. Ph. Buu-Hoi, B. Eckert, and R. Royer, J. Org. Chem. *17*, 1000 (1952).

Oxygen ↑ — RemC ⇅ O

Without additional reagents — *w.a.r.*

Organotin compounds
Cyanides from hydroxides — SnOH → SnCN

714. $$(C_6H_5)_3SnOH + HCN \rightarrow (C_6H_5)_3SnCN$$

Pure triphenyltin hydroxide allowed to stand some time with a large excess of anhydrous HCN (from KCN and concd. H_2SO_4), with occasional shaking → triphenyltin cyanide. Y: 95%. H. Zimmer and K. Lübke, B. *85*, 1119 (1952).

Lithium — *Li*

Synthesis of silanes from alkoxysilanes ←

715. $$(1\text{–}C_{10}H_7)_2Si(OC_2H_5)_2 \rightarrow (1\text{–}C_{10}H_7)_2Si(C_6H_5)_2$$

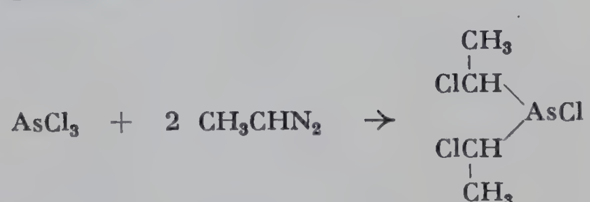
An ethereal soln. of di-1-naphthyldiethoxysilane added to excess phenyl-Li, and refluxed 1 hr. → di-1-naphthyldiphenylsilane. Y: 97%. F. e. s. H. Gilman and C. G. Brannen, Am. Soc. *73*, 4640 (1951).

Nitrogen ↑ — RemC ⇅ N

Without additional reagents — *w.a.r.*

Organometallic compounds
from diazo compounds ←

716.



A soln. of diazoethane in benzene added dropwise 1 hr. at 0-5° to a soln. of $AsCl_3$ in dry benzene, and allowed to stand overnight → di-(α-chlorethyl)chlorarsine. Y: 40%. F. e. s. A. Y. Yakubovich et al., Ж. *22*, 1528 (1952); C. A. *47*, 8010c; Ж. *22*, 1534 (1952); C. A. *47*, 9254g, and further papers of this series.

Sodium nitrite — *$NaNO_2$*

Selenocyanates from amines — NH_2 → SeCN

s. *7*, 664; s. a. L. Chierici and R. Passerini, Soc. *1954*, 3249

Cuprous bromide *CuBr*

Phosphonic and phosphinic acids from stable diazonium salts ←

717. 

PCl_3 and CuBr added to a stirred suspension of p-bromobenzenediazonium fluoborate in ethyl acetate, when the N_2-evolution has ceased water added, and the product isolated → p-bromobenzenephosphonic acid (startg. m. f. 526). Y: 61%.—Diarylphosphinic acids may be formed as by-products. G. O. Doak and L. D. Freedman, Am. Soc. *75*, 683 (1953); *73*, 5658 (1951); also in dioxane s. E. C. Ashby and G. M. Kosolapoff, Am. Soc. *75*, 4903 (1953); unsym. diarylphosphinic acid s. L. D. Freedman et al., Am. Soc. *75*, 1379 (1953).
Approximately the same yields are obtained with diazonium fluosilicates, but the reactions are less vigorous, and the products purified with less difficulty. L. D. Freedman and G. O. Doak, Am. Soc. *75*, 4905 (1953).

Halogen ↓ RemC⇅Hal

Without additional reagents *w.a.r.*

Tert. arsines R_3As

718. $$3\ F_3CI + As \rightarrow (F_3C)_3As$$

Finely ground arsenic and trifluoroiodomethane heated 48 hrs. at 220° in a sealed tube → tris(trifluoromethyl)arsine. Y: 70%. G. R. A. Brandt, H. J. Emeléus, and R. N. Haszeldine, Soc. *1952*, 2552 (1952).

Lithium *Li*

Organobismuth compounds ←

719. $$(C_6H_5)_3BiCl_2 + 2\ LiC_6H_5 \rightarrow (C_6H_5)_5Bi$$

1 *N* phenyl-Li soln. added dropwise with shaking at −75° under N_2 to a suspension of triphenyl-$BiCl_2$ in abs. ether, kept 1 hr. in the cooling bath, then allowed to come to room temp. with shaking, a few more drops of phenyl-Li soln. added, and the product isolated after 1 hr. → pentaphenylbismuth. Y: 81%. F. e. s. G. Wittig and K. Clauss, A. *578*, 136 (1952).

n-Butyllithium *n-C_4H_9Li*

Silanes from halogenosilanes SiHal → SiR
Halogen-metal interconversion

720.

An ethereal soln. of n-butyl-Li followed after 2 min. by an ethereal soln. of trimethylsilyl chloride added at 5° under N_2 to 3-bromodibenzothiophene in dry ether, then refluxed 2 hrs. with stirring → 3-trimethylsilyldibenzothiophene. Y: 80%. F. e. s. H. Gilman et al., Am. Soc. *73*, 5887, 4640 (1951).

Phosphines ←

s. *1*, 503; phenoxphosphine ring s. F. G. Mann and I. T. Millar, Soc. *1953*, 3746

Arsines ←

s. *1*, 504; s. a. J. Org. Chem. *19*, 1067 (1954)

Phenyllithium *C_6H_5Li*

Prim. phosphines from halides Hal → PH_2

721. $$C_6H_5CH_2Cl + LiPH_2 \rightarrow C_6H_5CH_2PH_2$$

Benzyl chloride added slowly with vigorous stirring and cooling to a suspension of monolithium phosphide, prepared from phenyl-Li and PH_3 in ether (Y: 98%) and cooled with Dry Ice-methanol, then allowed to warm to room temp. → benzylphosphine. Y: 75%. F. e. s. N. Kreutzkamp, B. *87*, 919 (1954).

Triphenylmethylsodium *$(C_6H_5)_3C\cdot Na$*

Silico-alkylation of carboxylic acid esters CH → $\mathrm{CSi}{<}$

722. $$(CH_3)_2CHCOOC_2H_5 + ClSi(CH_3)_3 \rightarrow (CH_3)_2C(Si(CH_3)_3)\cdot COOC_2H_5$$

Ethyl isobutyrate in ether, followed after 15 min. by trimethylchlorosilane in ether, added at room temp. to a stirred soln. of triphenylmethyl-Na in ether, stirring continued 1 hr., then allowed to stand for 12 hrs. → ethyl trimethylsilylisobutyrate. Y: 65% based on unrecovered ester. F. e. s. C. R. Hance and C. R. Hauser, Am. Soc. *75*, 994 (1953).

Magnesium *Mg*

Unsym. organomercury from monoörganomercury compounds RHgHal → RHgR′

723. $C_2H_5HgBr + BrCH_2CH{=}CH_2 \rightarrow C_2H_5HgCH_2CH{=}CH_2$

Ethyl-HgBr added below 5° in small portions with vigorous stirring to allyl-MgBr, and worked up when soln. is complete → allylethylmercury (startg. m. f. 594). Y: up to 60%. E. Rothstein and R. W. Saville, Soc. *1952*, 2987.

Phosphine oxides from halides ←

724. $2\ n{-}C_8H_{17}I + (n{-}C_4H_9O)_2P(O)H \rightarrow (n{-}C_8H_{17})_2P(O)H$

Di-n-butyl phosphite in dry ether added at 15° with stirring during ca. 50 min. to n-octyl-MgI in ether, then the temp. raised to the reflux point to complete the reaction → di-n-octylphosphine oxide (startg. m. f. 182). Y: 70%. F. e., with lower yields, s. R. H. Williams and L. A. Hamilton, Am. Soc. *74*, 5418 (1952).

Magnesium/zinc chloride *Mg/ZnCl₂*

Di- and mono-chlorophosphines ←

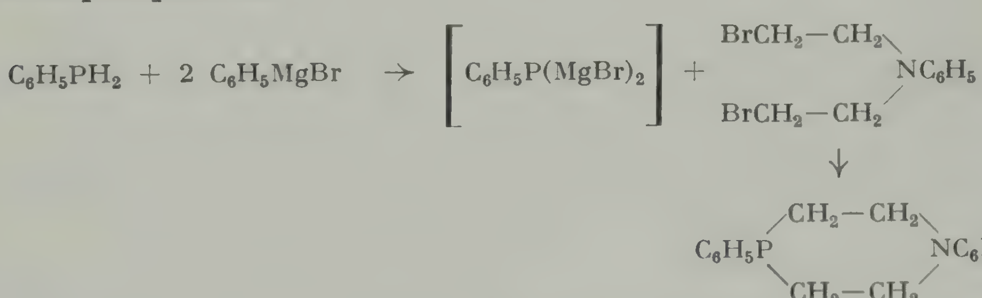
725. $C_6H_5Br \rightarrow [C_6H_5MgBr \rightarrow C_6H_5ZnCl] + PCl_3 \rightarrow C_6H_5PCl_2$

A soln. of freshly molten $ZnCl_2$ in ether added slowly in a N_2-stream with vigorous stirring to phenyl-MgBr in ether, stirring continued 15 min. at room temp., this mixture gradually driven by N_2 into a stirred soln. of PCl_3 in boiling ether, and refluxed 1 hr. with stirring → phenyldichlorophosphine. Y: 32.5%. F. e. s. T. Weil, B. Prijs, and H. Erlenmeyer, Helv. *35*, 1412 (1952); *36*, 1314 (1953); monochlorophosphines in low yields s. Helv. *37*, 654 (1954).

Phenylmagnesium bromide *C_6H_5MgBr*

1,4-Azaphosphorines ○

726.



In a N_2-atmosphere maintained throughout the reaction, a soln. of phenylphosphine in benzene added during 15 min. to ethereal phenyl-MgBr, refluxed 2.5 hrs. with stirring, whereby the ether is replaced by

benzene, to the resulting soln. of phenylphosphinebis(magnesium bromide) di-2′-bromoethylaniline in benzene added at 30° with vigorous stirring, and refluxed 2 hrs. → hexahydro-1,4-diphenyl-1.4-azaphosphorine. Y: 55%. F. G. Mann and I. T. Millar, Soc. *1952*, 3039.

Organomercury compounds ←

Synthesis of chlorophosphines from dichlorophosphines PCl → PR

727. $$C_6H_5PCl_2 \xrightarrow{(C_6H_5)_2Hg} (C_6H_5)_2PCl$$

A mixture of phenyldichlorophosphine and pure dry diphenyl-Hg heated 90 min. at 200° in an oil bath under a slow N_2-stream with occasional vigorous shaking, light petroleum (b.p. 60-80°) added, boiled 10 min., the petroleum decanted, the viscous residue mixed with half its bulk of dry sand, and the petroleum extraction continued → diphenylchlorophosphine (startg. m. f. 57). Y: 54%.—Omission of the treatment with sand gives lower yields, because the reaction product is not readily wetted by petroleum. F. G. Mann and I. T. Millar, Soc. *1952*, 4453.

Tetraalkyllead *R_4Pb*

Dichlorophosphines $RPCl_2$

s. *5*, 464; P^{32}-labeled compounds s. B. C. Saunders and T. S. Worthy, Soc. *1953*, 2115

Remaining Elements ↓ RemC⇅Rem

Potassium, sodium *K,Na*

Germanecarboxylic acids from digermanes $R_3GeGeR_3 \rightarrow 2\ R_3GeCOOH$

728. $$(C_6H_5)_3Ge\cdot Ge(C_6H_5)_3 \rightarrow 2\ (C_6H_5)_3GeCOOH$$

5:1 K-Na alloy followed by 25 drops of tetrahydrofuran added to a slowly stirred suspension of hexaphenyldigermane in ether, stirred 5-10 min., ether added, stirring continued for 24 hrs., then treated with Dry Ice-ether slurry → triphenylgermanecarboxylic acid (startg m. f. 195). Y: 83%. A. G. Brook and H. Gilman, Am. Soc. *76*, 77 (1954).

Mercuric chloride *$HgCl_2$*

Diarylmercury from aryllithium ←

s. *6*, 677; Hg-heterocyclics s. G. Wittig and W. Herwig, B. *87*, 1511 (1954)

Formation of C—C Bond

Uptake

Addition to Hydrogen and Carbon CC ⇓ HC

Potassium hydroxide *KOH*

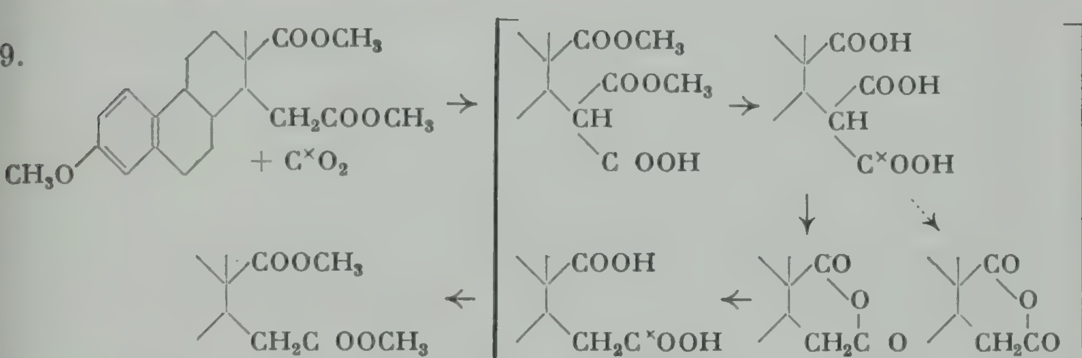
1,3-Diols from aldehydes ←
Tollens condensation

s. *4*, 613; also with CaO s. O. C. Dermer and P. W. Solomon, Am. Soc. *76*, 1697 (1954)

Triphenylmethylsodium *$(C_6H_5)_3C \cdot Na$*

Introduction of labeled carboxyl-C H → COOH
Malonic acid monoesters
from carboxylic acid esters

29.



Dimethyl marrianolate methyl ether dissolved in ether under N_2 in a special closed apparatus, treated successively with ethereal triphenyl-Na and $C^{14}O_2$ (generated from $BaC^{14}O_3$ with $HClO_4$), the crude product refluxed 2 hrs. with KOH in water-methanol, decarboxylated at 180° for 1 hr. in a slow N_2-stream, refluxed 1.5 hrs. with KOH in water-methanol to hydrolyze the anhydride formed during decarboxylation, and the diacid esterified with diazomethane in ether → labeled dimethyl marrianolate methyl ether. Y: 83% based on $BaC^{14}O_3$. M. Levitz, Am. Soc. *75*, 5352 (1953); introduction of labeled carboxyl-C s. a. C. J. Collins and B. M. Benjamin, Am. Soc. *75*, 1644 (1953).

Potassium carbonate *K_2CO_3*

Phenolcarboxylic acids from phenols
Marassé modification
of the Kolbe-Schmitt synthesis

s. *4*, 615; s. a. O. Baine et al., J. Org. Chem. *19*, 510 (1954)

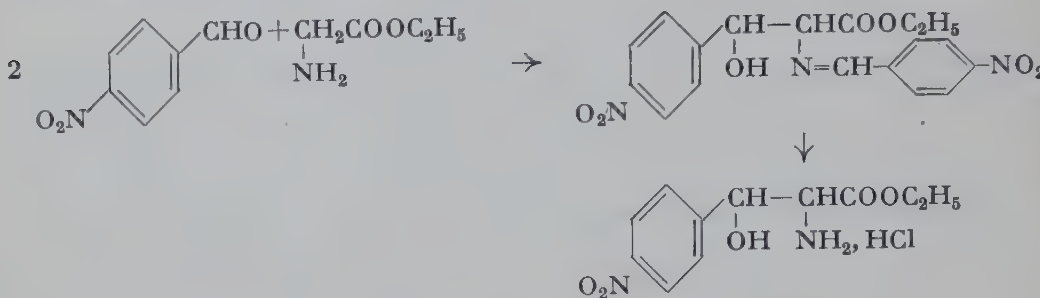
Addition to Oxygen and Carbon CC ⇓ OC

Without additional reagents *w.a.r.*

Synthesis of sec. alcohols from aldehydes CHO → CH(OH)R

s. *9*, 848

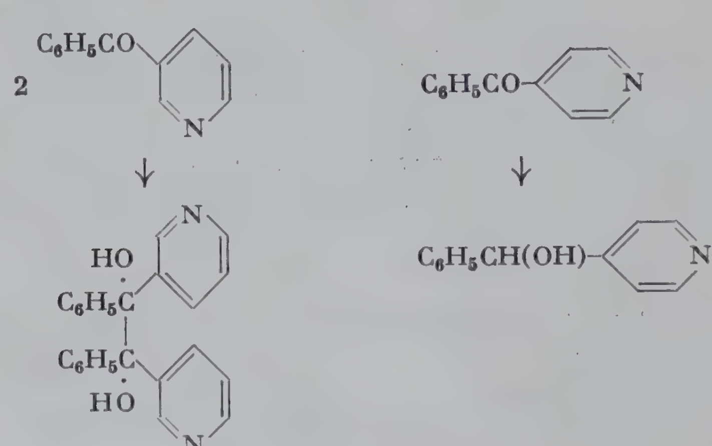
α-Amino-β-hydroxycarboxylic acid esters from aldehydes ←
Cleavage of azomethines

730.


A soln. of glycine ethyl ester in anhydrous methanol added to a soln. of p-nitrobenzaldehyde in warm methanol, kept 15 min. at 45°, then allowed to stand 48 hrs. at room temp. → ethyl N-p-nitrobenzylidene-β-(p-nitrophenyl)serinate (Y: 45.5%) suspended in abs. alcohol, then alcohol satd. with HCl-gas added, gently refluxed until soln. is complete, and allowed to stand 1 hr. at room temp. → ethyl *erythro*-β-(p-nitrophenyl)serinate hydrochloride (Y: 89.5%). G. Carrara et al., G. *82*, 325 (1952).

Irradiation/acetic acid ←

Pinacols and sec. alcohols from ketones by photoreduction ←

731.


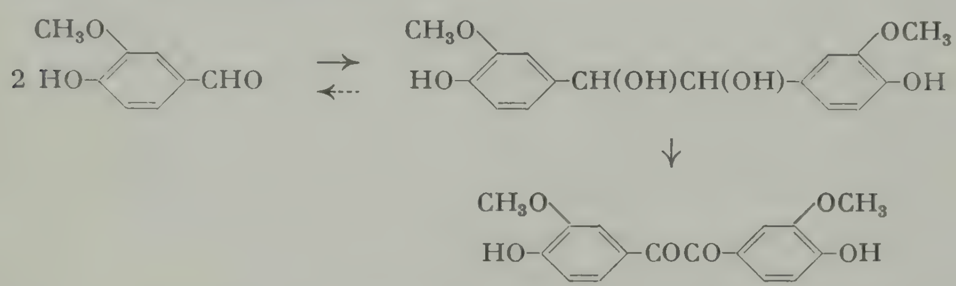
Phenyl 3-pyridyl ketone	Phenyl 4-pyridyl ketone
dissolved in 2-propanol, a drop of acetic acid added, and exposed in a sealed tube to direct sunlight for	
1 month → 1,2-di-(3-pyridyl)-1.2-diphenylethane-1.2-diol (startg. m. f. 797). Y: 68%.	2 months → phenyl-4-pyridylcarbinol. Y: 77%.—Although hydrols are the expected products of photochemical reduction in the presence of alkali, they have not been reported in its absence, as is the case here.

M. R. Kegelman and E. V. Brown, Am. Soc. *75*, 4649 (1953).

Electrolysis ↯

Benzils from aldehydes via hydrobenzoins ←
Aldehydes from hydrobenzoins

32.



A soln. of vanillin in aq. NaOH as catholyte electrolyzed 8.5 hrs. with Pb-electrodes using aq. NaOH as anolyte and a current of 3.6 amp. → hydrovanilloin (Y: 78%) mixed with $Cu(OH)_2$ and glacial acetic acid, then refluxed 1 hr. → vanillil (Y: 68%).—Oxidation in alkaline soln. gives vanillin, e.g. with Fehling soln. in quantitative yield. I. A. Pearl, Am. Soc. *74*, 4260 (1952).

Sodium hydroxide *NaOH*

α-Hydroxymethylketones from ketones H → CH_2OH

s. *4*, 621; monohydroxymethylation s. a. D. D. Evans et al., Soc. *1954*, 1687

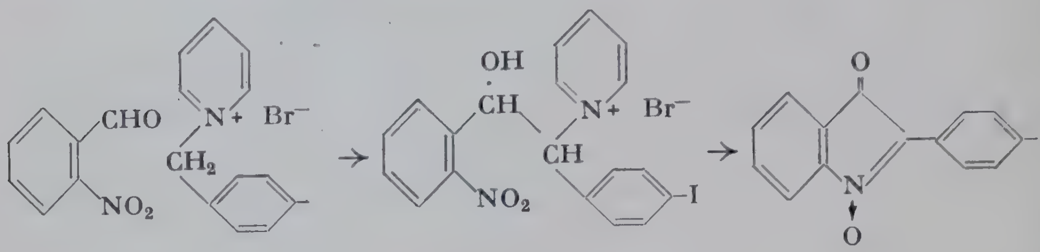
α-Amino-β-hydroxycarboxylic acids from aldehydes ←

s. *6*, 682; stereoisomers s. G. Ehrhart and J. Hennig, B. *87*, 892 (1954); K. N. F. Shaw and S. W. Fox, Am. Soc. *75*, 3421 (1953); with alc. KOH cf. W. A Bolhofer, Am. Soc. *76*, 1322 (1954); in KOH-melt s. T. Wieland, H. Cords, and E. Keck, B. *87*, 1312 (1954)

○

Isatogens from o-nitroaldehydes via quaternary cyclic β-hydroxyammonium salts

733.



10 N NaOH in 10 parts alcohol added at 0° to a soln. of p-iodobenzylpyridinium bromide and 2 moles o-nitrobenzaldehyde in a mixture of ethyl and methyl alcohols, and allowed to stand 12 hrs. at 3° in the dark → α-(p-iodophenyl)-β-(o-nitrophenyl)-β-hydroxyethylpyridinium bromide (Y: 95%) dissolved in 50%-acetic acid, and irradiated 2 hrs. with UV-light → 2-(p-iodophenyl)isatogen (Y: 93%). F. e. s. F. Kröhnke and I. Vogt, B. *85*, 368, 376 (1952).

Potassium hydroxide/acetal *KOH/RCH(OR')$_2$*

Acetylenealcohols from oxo compounds Syntheses with potassium hydroxide in solvents of the acetal type CO → C(OH)R

734. $2\ (CH_3)_2CO + HC{\equiv}CH \rightarrow (CH_3)_2C(OH){\cdot}C{\equiv}C{\cdot}C(OH)(CH_3)_2$

cf. Synth. Meth. *7*, 718

Acetylene passed at –10° into a suspension of KOH in methylal, then acetone added with continued introduction of acetylene whereby the temp. is allowed to rise to 20°, agitation continued for 5 hrs. → 2,5-dimethylhex-3-yne-2,5-diol. Y: 82%. F. e. s. E. D. Bergmann, M. Sulzbacher, and D. F. Herman, J. Appl. Chem. *3*, 39 (1953).

Sodium/alcohol *NaOR*

α-Nitroalcohols from ketones CO → C(OH)CH(NO$_2$)R

s. *7*, 685; s. a. Org. Synth. *34*, 19 (1954)

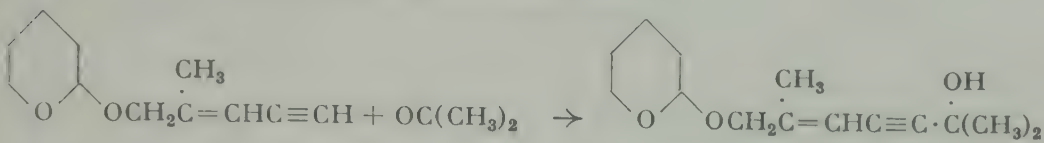
Potassium tert-pentoxide *KOR*

Ethynylalcohols from oxo compounds CO → C(OH)C⋮CH

s. *2*, 593; s. a. C. Djerassi et al., Am. Soc. *76*, 4092 (1954)

Phenyllithium *C_6H_5Li*

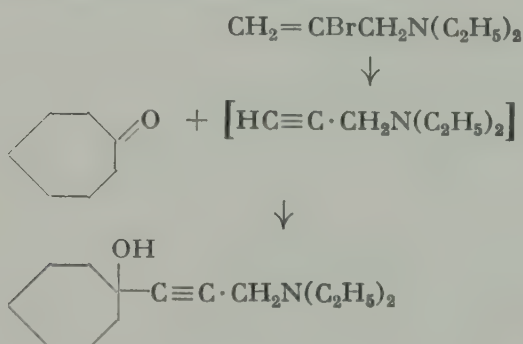
Synthesis of alcohols from oxo compounds

735.


An ethereal soln. of phenyl-Li added dropwise at 0° to an ethereal soln. of 2-methyl-1-tetrahydro-2′-pyranyloxypent-2-en-4-yne, after stirring at 0° for 7 hrs. acetone in ether added during 15 min., the temp. allowed to rise to 20° during 8 hrs., finally refluxed for 10 min. → 2,6-dimethyl-7-tetrahydro-2′-pyranyloxyhept-5-en-3-yn-2-ol. Y: 80%.—Lower yields were obtained with Mg. Also sec. alcohols from aldehydes s. R. Ahmad and B. C. L. Weedon, Soc. *1953*, 3286.

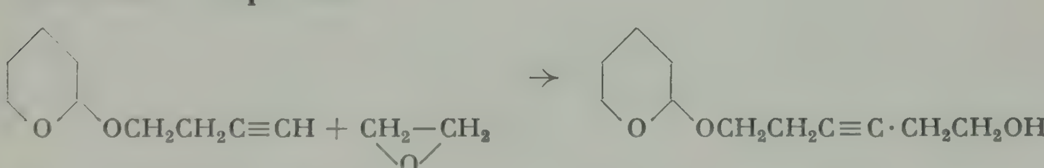
Lithium amide *$LiNH_2$*

Synthesis of acetylenealcohols from oxo compounds and α,β-ethylenebromides

736.


2-Bromo-3-diethylamino-1-propene added to a soln. of 2 moles $LiNH_2$ (from Li in the presence of ferric nitrate) in liq. NH_3, stirred 4 hrs., a soln. of cycloheptanone in dry ether then added dropwise during 30 min., stirring continued for a further 4 hrs., NH_4Cl added, and the NH_3 allowed to evaporate → 1-(3-diethylamino-1-propynyl)-1-cycloheptanol. Y: 72%. Also from acetylene derivatives s. A. M. Islam and R. A. Raphael, Soc. *1953*, 2247.

Synthesis of prim. acetylenealcohols from oxido compounds CH → $C \cdot CH_2CH_2OH$

737.


An ethereal soln. of 4-(tetrahydro-2-pyranyloxy)-1-butyne added dropwise during 15 min. to a stirred soln. of $LiNH_2$ (from Li in the presence of ferric nitrate catalyst) in liq. NH_3, stirring continued 40 min.,

then ethylene oxide added all at once, and stirred 9 hrs. → 6-(tetrahydro-2-pyranyloxy)-3-hexyn-1-ol. Y: 77%. R. A. Raphael and C. M. Roxburgh, Soc. *1952*, 3875.

Sodium/liq. ammonia *Na/NH_3*

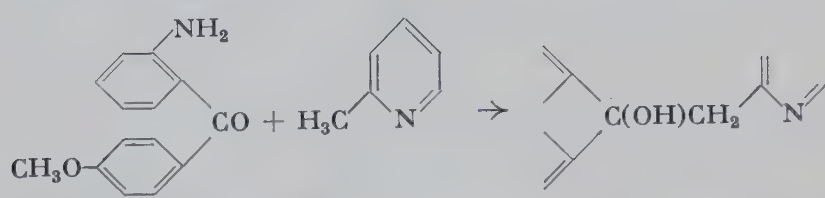
Ethynylalcohols from oxo compounds CO → C(OH)R

s. *4*, 624; s. a. D. Papa, F. J. Villani, and H. F. Ginsberg, Am. Soc. *76*, 4446 (1954)

Sodium amide *$NaNH_2$*

Tert. alcohols from ketones CO → C(OH)R

738.



2-Picoline added during 5 min. to a suspension of $NaNH_2$ in liq. NH_3, stirred 15 min., 2-amino-4′-methoxybenzophenone in 2-picoline and dry ether added during 10 min., and stirred 4 hrs. → 1-o-aminophenyl-1-p-methoxyphenyl-2,2′-pyridylethanol. Y: 49.6%. F. e. s. A. J. Nunn and K. Schofield, Soc. *1953*, 716.

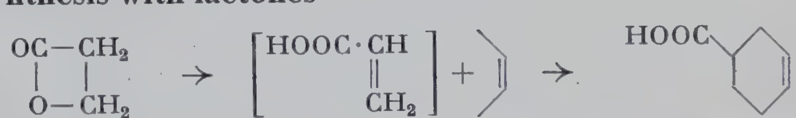
Ethynylalcohols from oxo compounds

s. *2*, 590; s. a. G. W. Stacy and R. A. Mikulec, Am. Soc. *76*, 524 (1954)

Potassium carbonate *K_2CO_3*

Diene synthesis with lactones ←

739.



β-Propiolactone can be used in place of acrylic acid as the dienophile component. K-carbonate, known to aid conversion of the lactone into acrylic acid is used as catalyst.—E: A mixture of β-propiolactone, butadiene, K-carbonate, and hydroquinone heated whereby exothermic reactions take place at ca. 100 and at ca. 200°, the temp. rising finally to 270° for a short time, the reaction completed by heating at 200° for 1.5 hrs. → cyclohexene-4-carboxylic acid. Y: 96%. F. e. s. T. L. Gresham, J. E. Jansen, and F. X. Werber, Am. Soc. *76*, 609 (1954).

Sodium cyanide *NaCN*

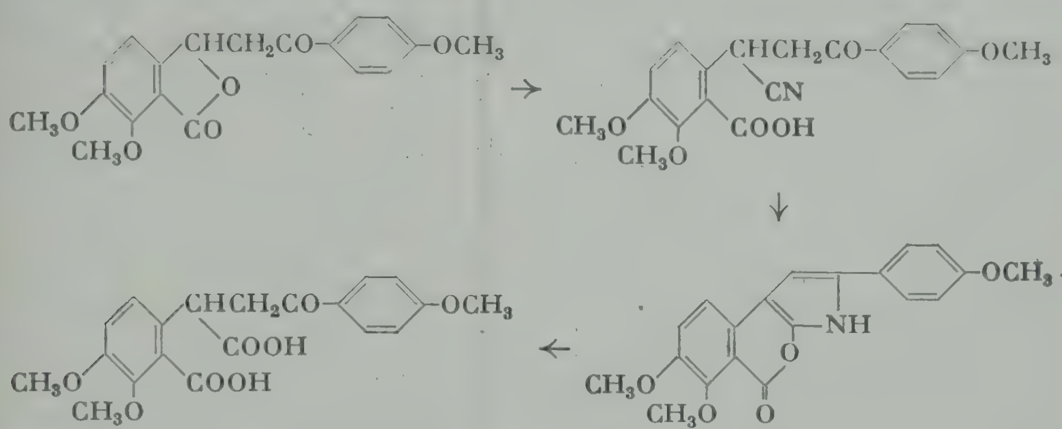
α-Cyanosulfonates from aldehydes CHO → $CH(CN)OSO_2R$

s. *9*, 663

Potassium cyanide *KCN*

Subst. homophthalic acids from phthalides via o-carboxyphenylacetonitriles and pyrrolo(2′,3′:3,4)isocoumarins ←

40.

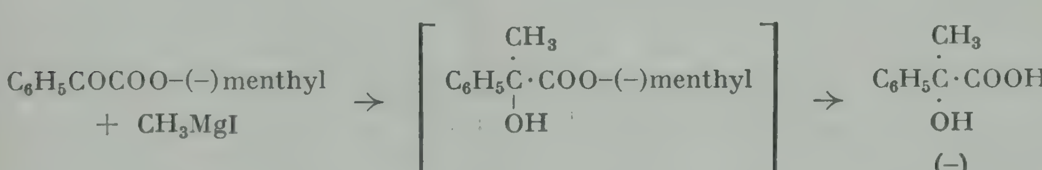


Na-acetate added to a soln. of 6,7-dimethoxy-3-(4-methoxyphenacyl)-phthalide in boiling 2-methoxyethanol, KCN in water added during 2 min. below the surface of the soln. heated in a boiling water bath, and heating continued 10 min. with gentle stirring every min. → α-(2-carboxy-3,4-dimethoxyphenyl)-β-(p-methoxybenzoyl)propionitrile (crude Y: 70%) dissolved in boiling glacial acetic acid, the source of heat removed, concd. HCl added, and heated 10 min. on a water bath → 7,8-dimethoxy-5′-(p-methoxyphenyl)pyrrolo(2′,3′:3,4)isocoumarin (3.4 g. from 5 g. phthalide), 5 g. heated 1.5 hrs. on a water bath with 10%-NaOH, then refluxed ca. 30 min. until NH_3-evolution ceases → 4.9 g. α-(2-carboxy-3,4-dimethoxyphenyl)-β-(p-methoxybenzoyl)propionic acid. F. e. s. A. S. Bailey and R. S. Staunton, Soc. *1952*, 2153.

Magnesium *Mg*

Asym. synthesis by Grignard reaction ←

41.



An ethereal soln. of (−)menthyl phenylglyoxylate (prepn. s. 359) added dropwise to ice-cooled ethereal methyl-MgI, allowed to stand 1 hr. at room temp., then gently refluxed for 30 min., and the crude product hydrolyzed by refluxing with KOH in methanol-water for 5 hrs. → (−)atrolactic acid. Y: 92%; optical Y: 25%. F. e. and theory s. V. Prelog et al., Helv. *36*, 320, 308, 325 (1953); s. a. C. F. Huebner and H. L. Troxell, J. Org. Chem. *18*, 736 (1953).

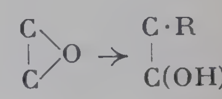
Tert. alcohols from ketones CO → C(OH)R

s. *9*, 981

Alkoxyacetylenealcohols CO → C(OH)R

s. *5*, 474; s. a. G. E. Arth et al., Am. Soc. *76*, 1715 (1954); H. Kappeler et al., Helv. *37*, 957 (1954)

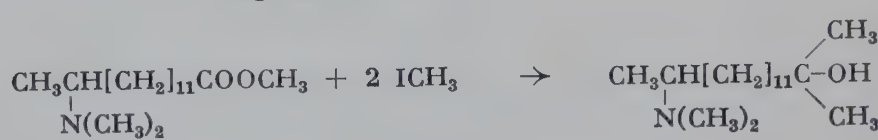
Sec. alcohols from oxido compounds



s. *5*, 476; s. a. P. Cagniant, Bl. *1952*, 970

Amino-tert-alcohols
from aminocarboxylic acid esters
Use of Trilon B in Grignard reactions COOR → $C(OH)R_2$

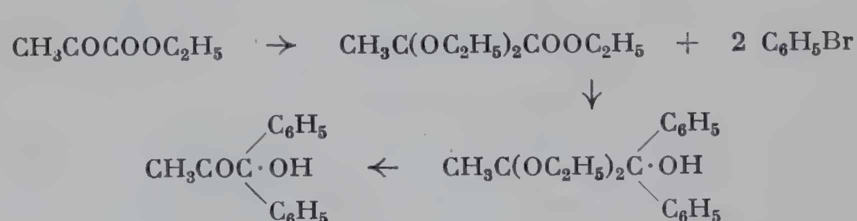
742.



Methyl 13-dimethylaminotetradecanoate allowed to react with methyl-MgI, then an aq. soln. of Trilon B (Na-ethylenediamine-N,N,N′,N′-tetraacetate) added at 40° → 14-dimethylamino-2-methyl-2-pentadecanol. Y: 78-85%.—The use of NH_4Cl for the removal of magnesium gives greatly lowered yields. J. Métivier, Bl. *1952*, 965.

Synthesis of hydroxyketones
from ketocarboxylic acid esters
Blocking of keto groups
by formation of acetals

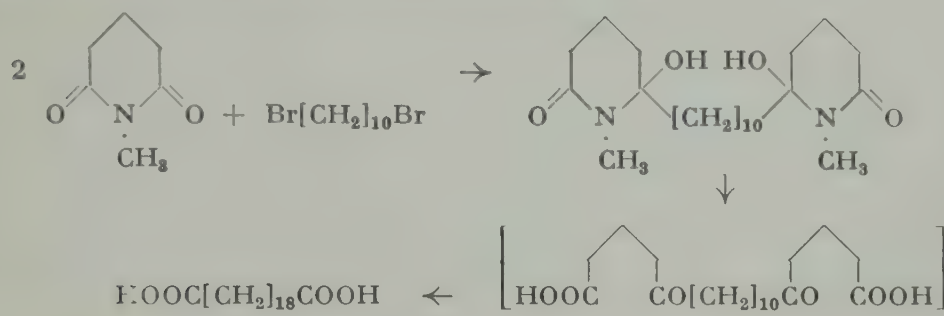
743.



A mixture of ethyl pyruvate, ethyl orthoformate, abs. ethanol, and 5 drops concd. H_2SO_4 allowed to stand 24 hrs., then refluxed 8 hrs. → ethyl α,α-diethoxypropionate (Y: 79%) added slowly with stirring and cooling during 2 hrs. to ethereal phenyl-MgBr, refluxed 2 hrs., and hydrolyzed with satd. NH_4Cl soln. → 1,1-diphenyl-2,2-diethoxy-1-propanol (Y: 61.5%) refluxed 3 hrs. with HCl in ethanol-water → α-hydroxy-α,α-diphenylacetone (Y: 98%) (startg. m. f. 626). C. L. Stevens and A. E. Sherr, J. Org. Chem. *17*, 1228 (1952).

Synthesis of long-chain α,ω-dicarboxylic acids ←
Carboxylic acids from
dicarboxylic acid imides
via α-hydroxylactams and ketocarboxylic acids

744.



α,ω-Decyl-di(MgBr) from α,ω-dibromodecane and Mg in abs. ether allowed to react with N-methylglutarimide → 1,10-bis-(1′-methyl-2′-hydroxy-6′-oxo-2′-piperidyl)-n-decane (Y: 26%) allowed to react with 100%-hydrazine hydrate in a soln. of Na in ethyleneglycol → octadecane-1,18-dicarboxylic acid. Y: 25%. F. e. s. R. Lukeš and K. Bláha. Collection Czechoslov. Chem. Communs. *18*, 804 (1953).

Synthesis of diols from lactones C

s. *5*, 477; s. a. G. Gamboni, H. Schinz, and A. Eschenmoser, Helv. *37*, 964 (1954)

Ethylmagnesium bromide C_2H_5MgBr

Acetylenealcohols from oxo compounds CO → C(OH)C⋮CR

in benzene s. 2, 599; s. a. K. R. Bharucha and B. C. L. Weedon, Soc. *1953*, 1584

Synthesis of hydroxysulfones CO → C(OH)R
from oxo compounds

745. $C_6H_5SO_2CH_3 \rightarrow [C_6H_5SO_2CH_2MgBr] + OHC{\cdot}C_6H_5 \rightarrow C_6H_5SO_2CH_2CH(OH)C_6H_5$

A soln. of methyl phenyl sulfone in dry benzene added during 10 min. to ethereal ethyl-MgBr, stirred 10 min., dil. with benzene, heated rapidly to the reflux temp. at which it is held for 3 min., cooled quickly, a soln. of benzaldehyde in dry benzene added with stirring during 1 hr. at 20-35°, and stirring continued 2 hrs. at room temp. → β-phenyl-β-hydroxyethyl phenyl sulfone. Y: 73-90%.—The hydroxysulfone could be converted in good yields to the corresponding keto, chloro, unsatd., and satd. sulfones. L. Field, Am. Soc. *74*, 3919 (1952); f. e. s. Am. Soc. *75*, 5582 (1953).

Phenylmagnesium bromide *C_6H_5MgBr*

Tert. alcohols from ketones
Polyfluoro compounds

746. $$(CH_3)_2CO + ICF_2CF_2CF_3 \rightarrow (CH_3)_2C(OH)CF_2CF_2CF_3$$

A soln. of phenyl-MgBr and a soln. of acetone both in anhydrous ether added simultaneously during 4 hrs. with ice-water cooling to an ethereal soln. of 1-iodoheptafluoropropane, and stirring continued for 8 hrs. at ice bath temp. → 3,3,4,4,5,5,5-heptafluoro-2-methyl-2-pentanol. Y: 65%. O. R. Pierce, A. F. Meiners, and E. T. McBee, Am. Soc. *75*, 2516 (1953).

Diethylaminomagnesium bromide *$(C_2H_5)_2MgBr$*

β-Hydroxycarboxylic acid esters from ketones $CO \rightarrow C(OH)CH_2COOR$

747. $$(C_6H_5)_2CO + CH_3COOCH(CH_3)_2 \rightarrow (C_6H_5)_2C(OH)CH_2COOCH(CH_3)_2$$

A soln. of benzophenone and isopropyl acetate in ether added dropwise at –5° with vigorous stirring to diethylamino-MgBr prepared from ethyl-MgBr and diethylamine, the temp. raised gradually to that of boiling, and refluxing continued 2 hrs. → isopropyl β,β-diphenylhydracrylate. Y: 86% based on benzophenone consumed. F. e. s. K. Sisido, H. Nozaki, and O. Kurihara, Am. Soc. *74*, 6254 (1952).

Zinc *Zn*

Reformatskii synthesis ←

s. *9*, 373

γ-Lactones from γ-ketocarboxylic acid esters ○

s. *5*, 479; s. a. A. S. Dreiding and A. J. Tomasewski, Am. Soc. *76*, 540 (1954)

Aluminum chloride *$AlCl_3$*

Prim. alcohols from oxido compounds

748. $$C_6H_6 + \underbrace{CH_2{-}CH_2}_{O} \rightarrow C_6H_5CH_2CH_2OH$$

Benzene treated with anhydrous $AlCl_3$, then ethylene oxide diluted with dry N_2 introduced at 6° with stirring at such a rate that 7-8 g./hr. are converted → β-phenethyl alcohol. Y: over 70%.—Solid hydrocarbons are dissolved in 4 parts methylene chloride or tetrachloroethane. F. e. s. H. Hopff and K. Koulen, B. *85*, 897 (1952).

Friedel-Crafts syntheses with succinic anhydride ←

s. *1*, 519; *3*, 566; *4*, 635a: with unsym.-subst. succinic anhydrides s. E. N. Marvell and A. O. Geiszler, Am. Soc. *74*, 1259 (1952); characterization of arenes s. J. D. Reinheimer and S. Taylor, J. Org. Chem. *19*, 802 (1954)

Amberlite ←

Catalysis with anion exchange resins ←
Nitroalcohols from nitroparaffins and aldehydes
Cyanoethylation

749.

$$CH_3CH_2CHO + CH_3NO_2 \rightarrow \underset{OH}{CH_3CH_2CHCH_2NO_2}$$

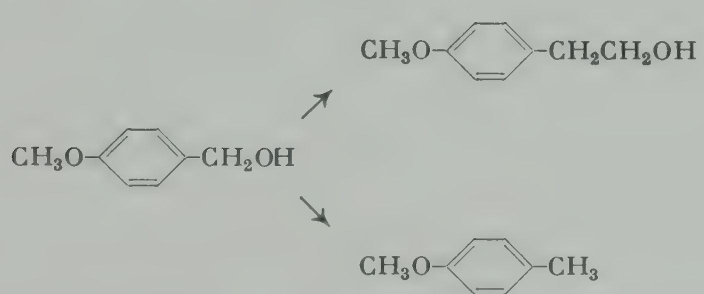
$$CH_2{=}CHCN \rightarrow C_2H_5OH \rightarrow C_2H_5OCH_2CH_2CN$$

A mixture of propionaldehyde, nitromethane, and ethanol passed during 3 hrs. at 27-30° through a column of Amberlite IRA-400 (hydroxyl form) → 1-nitro-2-butanol. Y: 70%.
Ethanol allowed to react with acrylonitrile in the presence of dry Amberlite IRA-400 → β-ethoxypropionitrile. Y: 90-93%. F. e. s. C. J. Schmidle and R. C. Mansfield, Ind. Eng. Chem. *44*, 1388 (1952).

Dicobalt octacarbonyl *$Co_2(CO)_8$*

Homologation of alcohols ←

750.



p-Methoxybenzyl alcohol and dicobalt octacarbonyl in benzene heated under an initial pressure of 238 atm. of synthesis gas (2 H_2: 1 CO), whereby gas absorption starts at ca. 70° and is essentially complete 35 min. later at 130° → 2-(p-methoxyphenyl)ethanol (Y: 44%) and p-methoxytoluene (Y: 16%). F. e. s. I. Wender et al., Am. Soc. *74*, 4079 (1952).

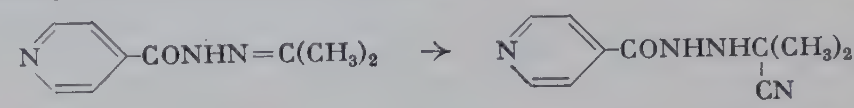
Addition to Nitrogen and Carbon — CC ⇓ NC

Without additional reagents — *w.a.r.*

Reactions of nitroacetic acid ester ←

s. *9*, 856

α-Cyanohydrazines from hydrazones — N:C → NHC·CN

751. 

A mixture of acetone isonicotinylhydrazone and liq. HCN kept 4 days at room temp. → 1-isonicotinyl-2-(1,1-dimethyl-1-cyanomethyl)hydrazine. Y: 72%. H. L. Yale et al., Am. Soc. *75*, 1933 (1953).

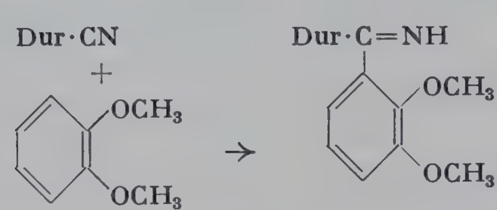
Potassium hydroxide — *KOH*

Quinoline from isatin ring ←
Pfitzinger-Borsche synthesis

s. *1*, 555; *2*, 603, 761; s. a. Soc. *1953*, 3768; H. R. Henze and D. W. Carroll, Am. Soc. *76*, 4580 (1954)

n-Butyllithium — *n-C_4H_9Li*

Synthesis of (hindered) ketimines from nitriles — CN → C(:NH)R

752. 

Veratrole in ether added to ethereal n-butyllithium (from Li and n-butyl chloride), refluxed 24 hrs., a soln. of duronitrile in ether added, heating continued overnight, and the product isolated as the hydrochloride → duryl 2,3-dimethoxyphenyl ketimine hydrochloride. Y: 77%. R. C. Fuson, W. D. Emmons, and J. P. Freeman, Am. Soc. *75*, 5321 (1953).

Potassium carbonate — *K_2CO_3*

α-Nitrocarboxylic acid amides from isocyanates — N:C:O → NHCOR

753. $$C_6H_5N{:}C{:}O + \underset{NO_2}{CH_2}COOC_2H_5 \rightarrow C_6H_5NHCO\underset{NO_2}{CH}COOC_2H_5$$

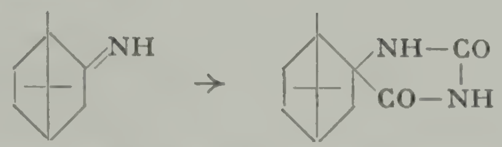
A mixture of ethyl nitroacetate, phenyl isocyanate, anhydrous K-carbonate, and dry benzene refluxed 3 hrs. → N-phenyl-α-carbethoxy-α-nitro-

acetamide. Y: 31%. F. e. s. R. N. Boyd and R. Leshin. Am. Soc. 75, 2762 (1953).

Potassium cyanide *KCN*

Hydantoins from imines ○

754.



Camphorimine nitrate, KCN, and NH_4-carbonate in 50%-ethanol warmed 5 hrs. at 52° → spiro(camphane-2,5′-hydantoin). Y: 86%.—The prepn. from camphor was unsuccessful. E. S. Rothman and A. R. Day, Am. Soc. 76, 111 (1954).

Diethylamine *$(C_2H_5)_2NH$*

1,2-Nitramines from azomethines N:C → NHCR

s. *9*, 413

Magnesium *Mg*

Sec. amines from azomethines C:NR → C(NHR)R′

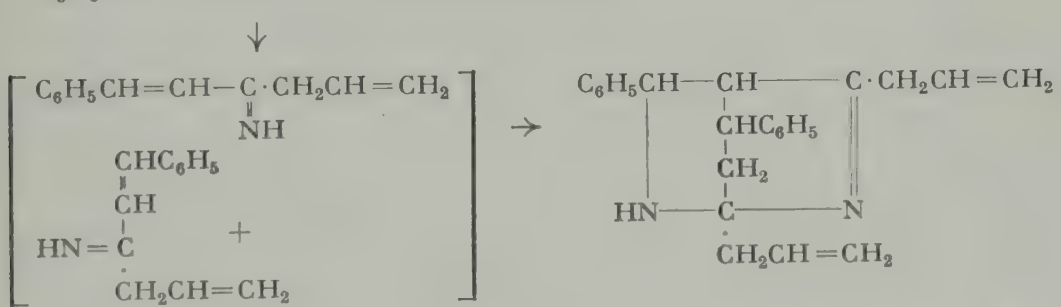
s. *4*, 643; s. a. Org. Synth. *34*, 64 (1954)

Synthesis of azomethines from nitriles ←

s. *9*, 756

Endopyrimidine ring from α,β-ethylenenitriles ○

755. 2 $C_6H_5CH{=}CHCN$ + 2 $CH_2{=}CHCH_2MgBr$

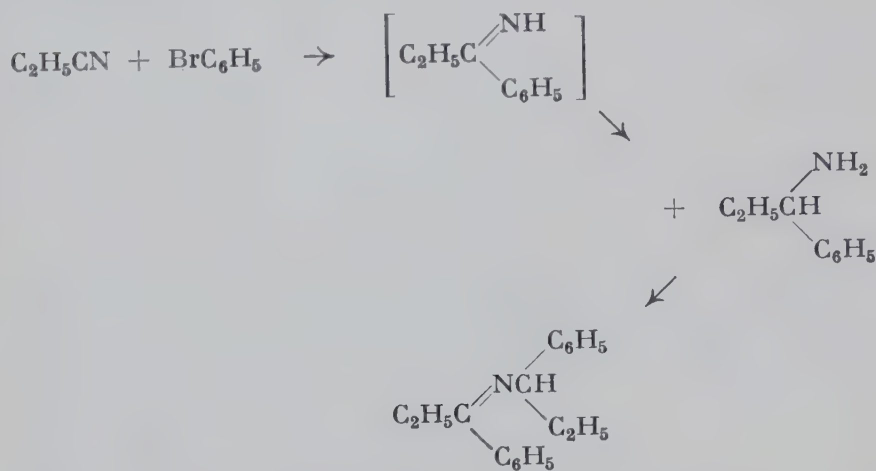


Cinnamonitrile added to allyl-MgBr, hydrolyzed with NH_4Cl-soln., and the product isolated as the hydrochloride → allyl styryl ketimine dimer dihydrochloride. Y: 88%. F. e. s. H. R. Henze and L. R. Swett, Am. Soc. 73, 4918 (1951).

Magnesium/lithium aluminum hydride *Mg/LiAlH₄*

←

Synthesis of amines and azomethines from nitriles

756. 

Propionitrile added dropwise with stirring to phenyl-MgBr from bromobenzene and Mg in ether, refluxed 2 hrs.,

a slurry of $LiAlH_4$ in tetrahydrofuran added slowly, refluxed 18 hrs.,	1-phenylpropylamine added dropwise, refluxed 3 hrs. with stirring,

then decomposed with cooling by careful addition of water and aq. NaOH

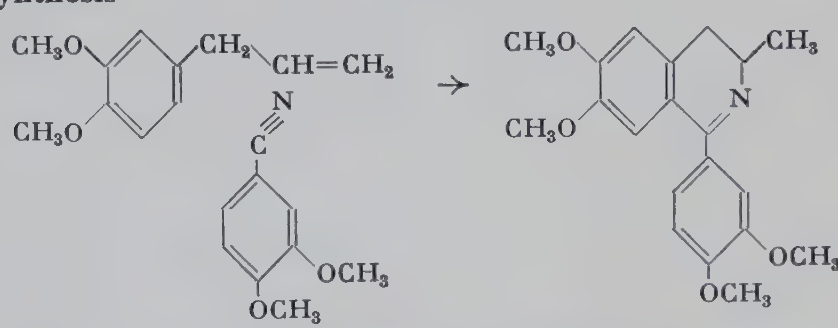
→ 1-phenylpropylamine. Y: 80%.	→ N-(1-phenylpropyl)-1-phenylpropylidenimine. Y: 74%.

F. e. s. A. Pohland and H. R. Sullivan, Am. Soc. 75, 5898 (1953).

Sulfuric acid *H_2SO_4*

3,4-Dihydroisoquinolines from nitriles
New synthesis

○

757. 

Veratronitrile added portionwise with rapid stirring to concd. H_2SO_4 in an ice bath, which is removed after the addition, methyleugenol then added during 2 min. whereby the rapidly rising temp. is maintained around 80° by intermittent cooling, allowed to stand 3 days at room

temp. → 1-(3',4'-dimethoxyphenyl)-3-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline. Y: 53%. F. e. s. J. J. Ritter and F. X. Murphy, Am. Soc. *74*, 763 (1952).

Addition to Carbon — CC ⇓ CC

Without additional reagents — *w.a.r.*

Synthesis of polyhalides ←

758. $$CF_3CF_2I + HC{\equiv}CH \rightarrow CF_3CF_2CH{=}CHI$$
$$CF_3I + CH_2{=}CH_2 \rightarrow CF_3CH_2CH_2I$$

Pentafluoroiodoethane heated with 20% excess acetylene at 220-260° for 15-20 hrs. in a sealed tube → 3,3,4,4,4-pentafluoro-1-iodo-1-butene. Y: 72%.—Trifluoroiodomethane heated with ethylene at 275° for 15 hrs. in an autoclave → 1,1,1-trifluoro-3-iodopropane. Y: 82% based on startg. m. consumed. R. N. Haszeldine and K. Leedham, Soc. *1952*, 3483; *1953*, 1548; *1954*, 2040.

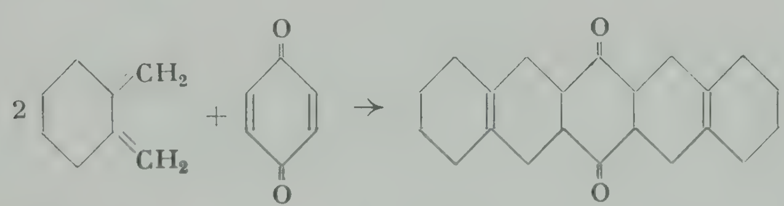
Reaction of oxalyl chloride with unsatd. compounds ←
α,β-Ethylenecarboxylic acids from ethylene derivatives

759. $$(C_6H_5)_2C{=}CH_2 + (COCl)_2 \rightarrow [(C_6H_5)_2C{=}CHCOCl] \rightarrow (C_6H_5)_2C{=}CHCOOH$$

Diphenylethylene and oxalyl chloride gently refluxed for 3-4 hrs., dil. with benzene, and extracted with Na-carbonate soln. → β-phenylcinnamic acid. Y: 50%. F. e. and limitations s. M. S. Kharasch, S. S. Kane, and H. C. Brown, Am. Soc. *64*, 333 (1942); s. a. W. Tadros, Y. Akhnookh, and G. Aziz, Soc. *1953*, 186.

Diene synthesis ○
Diels-Alder reaction

760.



Linear annulization. A soln. of 1,2-dimethylenecyclohexane and benzoquinone in dioxane refluxed 2 hrs. until a precipitate is formed, then refluxed an additional hr. → 6,13-diketo-$\Delta^{1a(14a),7a(11a)}$-octadecahydropentacene. Y: 77%. W. J. Bailey and M. Madoff, Am. Soc. *75*, 5603 (1953).

Isocyclics from acetylene derivatives

s. *7*, 712; *8*, 735; s. a. W. J. Bailey, J. Rosenberg, and L. J. Young, Am. Soc. *76*, 2251 (1954)

with furan

s. *3*, 704; s. a. G. Stork et al., Am. Soc. *75*, 384 (1953)

with nitro compounds

s. *9*, 299

Dihydropyrans from
α,β-ethyleneoxo compounds

s. *6*, 696; s. a. Am. Soc. *75*, 1312 (1953)

Pyrazolines from ethylene derivatives
and diazo compounds

s. *5*, 490; *7*, 713; *8*, 737; steroid derivatives s. G. P. Mueller and B. Riegel, Am. Soc. *76*, 3686 (1954)

Irradiation ←

Free radical additions C:C → CHalCR
Synthesis of polyhalides

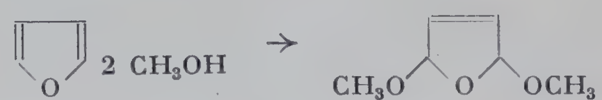
761. $$CF_3CH{=}CH_2 + CCl_3Br \rightarrow CF_3CHBrCH_2CCl_3$$

A mixture of 1,1,1-trifluoro-2-propene and bromotrichloromethane irradiated 24 hrs. with a mercury flood lamp in a quartz ampule held horizontally to permit irradiation of both liquid and vapor phases → 2-bromo-4,4,4-trichloro-1,1,1-trifluorobutane. Y: 76%. F. e. s. A. L. Henne and M. Nager, Am. Soc. *73*, 5527 (1951); s. a. R. N. Haszeldine, Soc. *1952*, 2504.

Electrolysis ↯

Alkoxylation of furans ←

762.



A mixture of furan, methanol, and NH_4Br electrolyzed ca. 16 hrs. at −22° with a brass-nickel cathode, a Pt-anode, a current of 3.0-2.3 amp., and a potential of 4.6-5.3 v. → 2,5-dimethoxy-2,5-dihydrofuran. Y: 73%. N. Clausen-Kaas, Acta Chem. Scand. *6*, 531 (1952); f. e. s. the following papers of this series.

Sodium *Na*

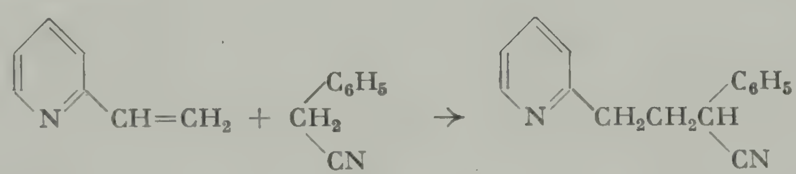
C-Cyanoethylation H → CH_2CH_2CN

763. $C_6H_5CH_2COCH_3 + CH_2{=}CHCN \rightarrow C_6H_5CH(CH_2CH_2CN)COCH_3$

Na added to phenylacetone, stirred and heated at 95° until the Na melts, then the reaction allowed to proceed without external heating for ca. 5 min. until the Na has dissolved, at 80° acrylonitrile added dropwise with water cooling during 15 min., and stirring continued for 15 min. → γ-phenyl-γ-acetobutyronitrile. Y: 80%. E. D. Bergmann and J. Szmuszkovicz, Am. Soc. *75*, 3226 (1953); esters s. V. Boekelheide et al., Am. Soc. *75*, 3243 (1953).

Pyridylethylation ←

764.



2-Vinylpyridine added dropwise with stirring at 150-160° to phenylacetonitrile containing Na, and stirring continued 5 hrs. at 160-170° → α-phenyl-γ-(2-pyridyl)butyronitrile. Y: 77%. F. e. s. V. Boekelheide et al., Am. Soc. *75*, 3243 (1953).

s. *7*, 716; s. a. Am. Soc. *75*, 1368 (1953)

Sodium hydroxide *NaOH*

C-Cyanoethylation of aldehydes H → CH_2CH_2CN

s. *9*, 768

Sodium/alcohol *NaOR*

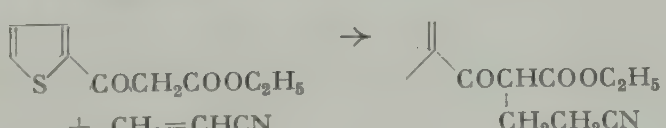
Michael addition ←

s. *5*, 493; s. a. H. Kappeler et al., Helv. *37*, 957 (1954)

C-Cyanoethylation H → CH_2CH_2CN

γ-Cyanoketones and δ-ketocarboxylic acids from β-ketocarboxylic acid esters via α-cyanoethyl-β-ketocarboxylic acid esters

765.



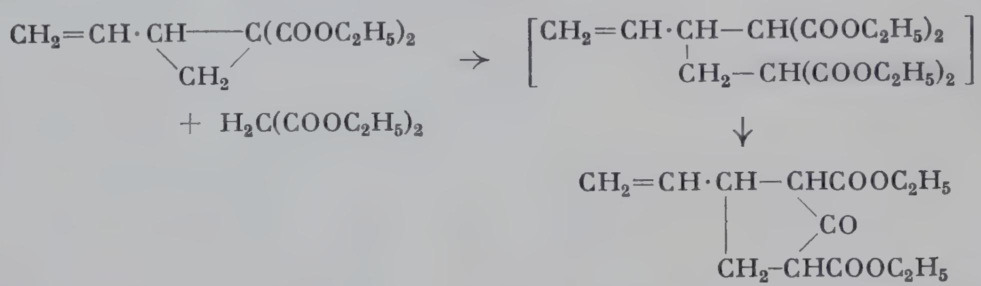
Acrylonitrile added with rapid stirring to a soln. of Na and ethyl 2-thenoylacetate in 95%-ethanol at a rate to keep the temp. at 40-45°, then

allowed to cool to room temp. during 30-60 min. → ethyl α-(β-cyanoethyl)-2-thenoylacetate. Y: 64%. F. e., also hydrolysis to γ-cyanoketones and δ-ketoacids, s. C. W. Yoho and R. Levine, Am. Soc. *74*, 5597 (1952); C-cyanoethylation of α-cyanocarboxylic acid esters s. M. S. Newman and J. L. McPherson, J. Org. Chem. *19*, 1717 (1954).

Michael addition ○
Cyclohexanediones

s. *6*, 703; s. a. K. W. Rosenmund, H. Herzberg, and H. Schütt, B. *87*, 1258 (1954)

Cyclopentanones from cyclopropanes ←

766. 

Ethyl malonate added to a stirred soln. of Na in alcohol, refluxed 0.5 hr., ethyl 2-vinylcyclopropane-1,1-dicarboxylate added, and heating continued overnight → ethyl 2-keto-4-vinylcyclopentane-1,3-dicarboxylate. Y: 54%. R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, Soc. *1952*, 3616.

Potassium hydroxide/alcohol *KOH*

C-Cyanoethylation of 1,1-disulfones H → CH_2CH_2CN

767. $(CH_3)_2CHCH_2CH_2CH(SO_2C_2H_5)_2 + CH_2{=}CHCN \rightarrow (CH_3)_2CHCH_2CH_2C(SO_2C_2H_5)_2CH_2CH_2CN$

1,1-Bis(ethylsulfonyl)-4-methylpentane (prepn. s. 880) added to *tert*-butanol containing KOH and acrylonitrile, whereupon the temp. rises to 40-45°, allowed to stand 6 hrs. at this temp. → 4,4-bis(ethylsulfonyl)-7-methyloctanonitrile. Y: 95%. F. e. s. M. W. Cronyn, Am. Soc. *74*, 1225 (1952).

Potassium cyanide *KCN*

C-Cyanoethylation of aldehydes

768. $(CH_3)_2CHCHO + CH_2{=}CHCN \rightarrow (CH_3)_2C(CHO)CH_2CH_2CN$

25%-KCN soln. added dropwise during 1 hr. with vigorous stirring to a mixture of isobutyraldehyde and acrylonitrile containing a little hydroquinone heated at 80° under a slight N_2 pressure, which is then

slowly released while heating is continued for 1 hr. at 80-90° → α,α-dimethyl-γ-cyanobutyraldehyde. Y: 79%. D. Hoch and P. Karrer, Helv. *37*, 397 (1954); with NaOH in lower yields s. H. Born, R. Pappo, and J. Szmuszkowicz, Soc. *1953*, 1779.

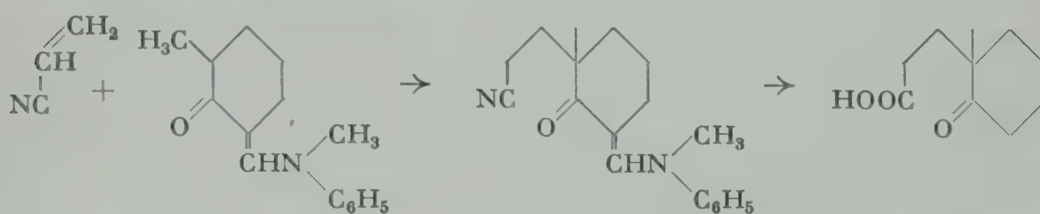
Subst. succinic acids C:C → CHC(CN)

s. *6*, 705; s. a. C. A. Miller and L. M. Long, Am. Soc. *75*, 373, 6256 (1953)

Triton B ←

C-Cyanoethylation
Carboxylic acids from nitriles
Blocking of ketone α-positions H → CH_2CH_2CN

769.



A ca. 3.5% soln. of Triton B in t-butanol containing some water added to a soln. of 2-methylanilinomethylene-6-methylcyclohexanone in t-butanol, then acrylonitrile and a trace of hydroquinone added, allowed to stand 22 hrs. at room temp. under N_2, and the crude product heated 7 hrs. with aq. KOH under N_2 → 2-(β-carboxyethyl)-2-methylcyclohexanone. Y: 81%.—By the addition of water, the polymerization of acrylonitrile is suppressed. F. e. s. R. B. Woodward et al., Am. Soc. *74*, 4223 (1952).

Pyridylethylation ←

with Na s. *7*, 716; also with Triton B. s. Am. Soc. *75*, 1368 (1953)

Diethylamine $(C_2H_5)_2NH$

Synthesis of aliphatic nitro compounds from ethylene derivatives C:C → CHCR

s. *4*, 656; s. a. A. Dornow and F. Boberg, A. *578*, 101 (1952)

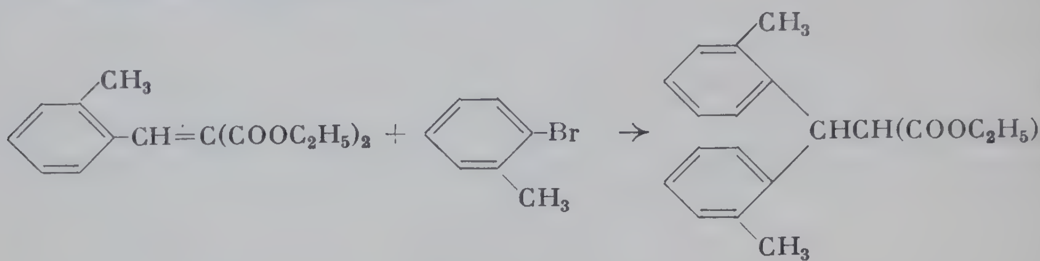
Calcium carbide/nickel acetylacetonate ←

s. Nickel acetylacetonate/calcium carbide

Magnesium *Mg*

Addition of Grignard reagents to carbon-carbon double bonds C:C → CHCR

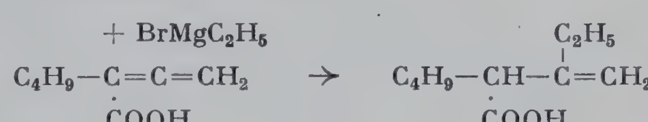
770.



A soln. of ethyl 2-methylbenzalmalonate in ether added dropwise during 1 hr. at 0-5° to a well-stirred soln. of o-tolyl-MgBr in ether, and stirring continued 2 hrs. at room temp. → ethyl 2,2′-dimethylbenzhydrylmalonate. Y: 72%. F. e. s. M. S. Newman and M. Wolf, Am. Soc. *74*, 3225 (1952).

Synthesis of β,γ-ethylenecarboxylic acids from α-allenecarboxylic acids and of carboxylic acids from α,β-ethylenecarboxylic acids

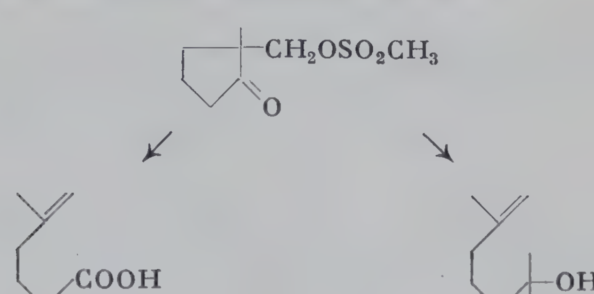
771.



A soln. of 1,2-heptadiene-3-carboxylic acid in dry ether added with shaking to 2.5 moles ethyl-MgBr in ether, the resulting soln. poured on Dry Ice, and upon coming to room temp. hydrolyzed with satd. NH_4Cl-soln. → 2-butyl-3-ethyl-3-butenoic acid. Y: 85%. J. H. Wotiz and J. S. Matthews, Am. Soc. *74*, 2559 (1952); carboxylic acids from α,β-ethylenecarboxylic acids, in lower yields, s. Am. Soc. *75*, 6342 (1953).

Hydrolytic ring opening of isocyclics with simultaneous formation of ethylene derivatives from sulfonic acid esters ←

772.



2-Hydroxymethyl-2-methylcyclopentanone mesylate

refluxed 0.5 hr. at 125-130° with aq. 40%-KOH, water added and boiling continued for 3 hrs. → 5-methylene-hexanoic acid. Y: 82%.

dissolved in ether-tetrahydrofuran, added dropwise with vigorous stirring and ice-cooling to ethereal methyl-MgI, and refluxed 3 hrs. → 2-methyl-6-methylene-2-heptanol. Y: 81%.

A. Eschenmoser and A. Frey, Helv. *35*, 1660 (1952).

Aluminum amalgam *Al,Hg*

Reductive dimerization ←

773. $2\ \underset{CH_3}{CH}=C(COOC_2H_5)_2 \rightarrow (C_2H_5OOC)_2CH\underset{CH_3}{CH}-\underset{CH_3}{CH}CH(COOC_2H_5)_2$

Amalgamated Al-foil covered with ether, diethyl ethylidenemalonate added with stirring during 30 min., water added when the vigorous reaction has subsided, and stirred overnight → tetraethyl 2,3-dimethylbutane-1,1,4,4-tetracarboxylate. Y: 81%. L. Crombie, J. E. H. Hancock, and R. P. Linstead, Soc. *1953*, 3496.

Boron fluoride *BF_3*

1,3-Diol ethers from ethylene derivatives and acetals ←

774. $C_6H_5CH=CH_2 + CH_2(OCH_3)_2 \rightarrow C_6H_5\underset{OCH_3}{CH}CH_2CH_2OCH_3$

A large excess of methylal treated with BF_3, then styrene added with vigorous stirring, and the product isolated after 1 hr. at 25° → 1,3-dimethoxy-1-phenylpropane. Y: 72%.—Orientation corresponds to that in the analogous Prins reaction of aldehydes and olefins. F. e., with lower yields, s. O. C. Dermer and J. J. Hawkins, Am. Soc. *74*, 4595 (1952).

Aluminum chloride *$AlCl_3$*

Synthesis of hydrocarbons from ethylene derivatives Eijkman reaction C:C → CHCR

s. *4*, 659; s. a. S. M. Mukherji, V. S. Gaind, and P. N. Rao, J. Org. Chem. *19*, 328 (1954); naphthalene derivatives s. J. Colonge and R. Domenech, Bl. *1952*, 1000

Diethylamine acetate ←

Benzene ring by trimerization ○

775.

Butinone heated 10 min. on a water bath with diethylamine acetate → sym-triacetylbenzene. Y: 34%. F. Wille and F. Knörr, B. *85*, 841 (1952).

Acetic anhydride *$(CH_3CO)_2O$*

Nitriles from ethylene derivatives C:C → CHC(CN)

776.

An aq. soln. of 2 moles KCN added dropwise with stirring to a soln. of 1 mole 2-vinylpyridine and 2 moles acetic anhydride at a rate to maintain gentle boiling, then heated 16 hrs. with stirring on a steam bath → β-(2-pyridyl)propionitrile. Y: 67%. V. Boekelheide et al., Am. Soc. *75*, 3243 (1953).

Benzoyl peroxide *$(C_6H_5COO)_2$*

Free radical reactions ←
Synthesis of ketones
from aldehydes and ethylene derivatives

s. *8*, 745; s. a. Org. Synth. *34*, 51 (1954); Ng. Ph. Buu-Hoï, R. *72*, 84 (1953)

Sulfuric acid *H_2SO_4*

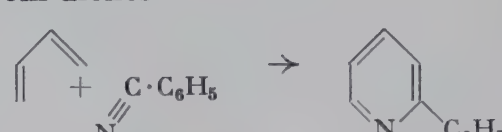
Alkylation with ethylene derivatives
Isocyclics ←

s. *5*, 506, s. a. W. L. Lenneman, R. D. Hites, and V. I. Komarewsky, J. Org. Chem. *19*, 463 (1954)

Chromium oxide/alumina *Cr_2O_3/Al_2O_3*

Pyridine ring from dienes ○

777.



Benzonitrile and butadiene passed at 400° during 4 sec. over a 4%-Cr_2O_3/Al_2O_3 catalyst → 2-phenylpyridine. Y: 60%. G. J. Janz, W. J. G. McCulloch, and E. F. Timpane, Ind. Eng. Chem. *45*, 1343 (1953).

Nickel acetylacetonate/calcium carbide ←

Subst. cycloöctatetraenes ○
by copolymerization

78.

A mixture of 1-pentyne, dry tetrahydrofuran, Ni-acetylacetonate, and powdered Ca-carbide heated 7-12 hrs. at 70-90° and an acetylene pressure of 300-150 p. s. i. → n-propylcycloöctatetraene. Y: 25%. F. e., with lower yields, s. A. C. Cope and H. C. Campbell, Am. Soc. *74*, 179 (1952).

Nickel carbonyl *$Ni(CO)_4$*

Carbonylation ←

s. *3*, 588; s. a. A. *582*, 1-116 (1953)

Via intermediates *v.i.*

Cyanoethylation of ketones H → CH_2CH_2CN
via enamines

s. *9*, 912

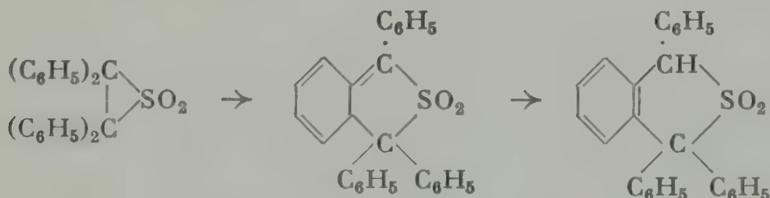
Rearrangement

Hydrogen/Carbon Type CC⌒HC

Without additional reagents *w.a.r.*

Isomerization of cyclic sulfones ←
Aromatization by migration
of a carbon-carbon double bond

79.

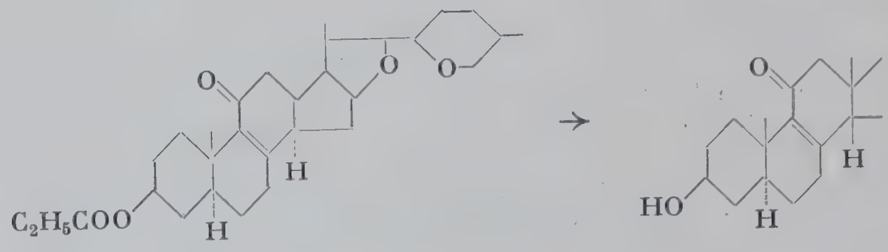


A suspension of tetraphenylthiirane 1,1-dioxide in CS_2 refluxed 15 min. → 1,1,3-triphenyl-1,7a-dihydroisothianaphthene 2,2-dioxide (Y: 75%) dissolved in acetone, and treated with 3 drops of pyridine → 1,1,3-triphenyl-1,3-dihydroisothianaphthene 2,2-dioxide (Y: 90%). H. Kloosterziel and H. J. Backer, R. *71*, 1235 (1952).

Potassium hydroxide *KOH*

Epimerization of steroids ←

780.



A soln. of 3.5 g. Δ^8-22a-5α-spirosten-3β-ol-11-one propionate refluxed 1 hr. with methanolic 5%-KOH → 2.8 g. Δ^8-22a-5α-14-iso(β)-spirosten-3β-ol-11-one. C. Djerassi et al., Am. Soc. *75*, 3496 (1953); 9α- from 9β-H-atoms s. J. Elks et al., Soc. *1953*, 2933.

Sodium/alcohol *NaOR*

Migration of carbon-carbon double bonds ←

781. $C_6H_5SCH_2CH{=}CH_2 \rightarrow C_6H_5SCH{=}CHCH_3$

Allyl phenyl sulfide refluxed 12 hrs. in a soln. of Na in abs. alcohol under N_2 → propenyl phenyl sulfide (mixture of cis- and trans-isomers). Y: 95%. F. e. s. D. S. Tarbell and M. A. McCall, Am. Soc. *74*, 48 (1952).

α,β- from β,γ-Ethyleneketones

s. *9*, 87

Pyridine *C_5H_5N*

Aromatization by migration of carbon-carbon double bonds

s. *9*, 779

Cuprous bromide *CuBr*

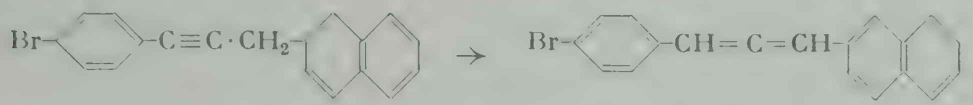
Allenes from acetylene derivatives ←

782. $HC{\equiv}C{\cdot}CH_2Br \rightarrow H_2C{=}C{=}CHBr$

3-Bromopropyne stirred with solid CuBr while it is slowly distilled through a good fractionating column → bromopropadiene. Y: 55-65%. T. L. Jacobs and W. F. Brill, Am. Soc. *75*, 1314 (1953).

Aluminum oxide *Al_2O_3*

783.

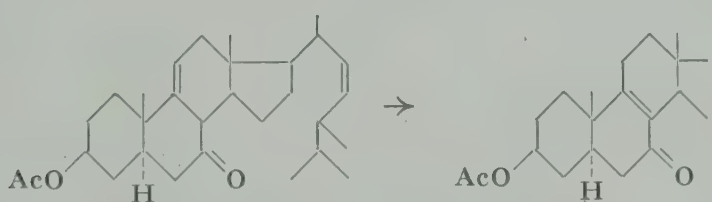


1-(p-Bromophenyl)-3-(β-naphthyl)-1-propyne adsorbed from its soln. in n-heptane on a column containing dry, activated alumina, the adsorbent covered with a little n-heptane, the column stoppered and allowed to stand 8 hrs. at room temp. → 1-(p-bromophenyl)-3-(β-naphthyl)allene. Y: 50%.—This is the first example of a 1,3-diarylallene to appear in the literature. T. L. Jacobs and S. Singer, J. Org. Chem. *17*, 475 (1952).

Boron fluoride *BF_3*

α,β- from β,γ-Ethyleneketones ←
Steroids

784.



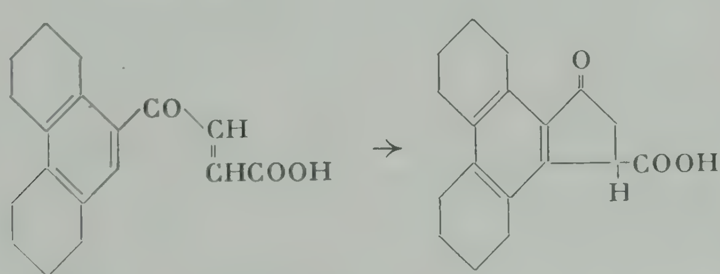
80 mg. 3β-acetoxy-7-oxo-$\Delta^{9(11),22}$-ergostadiene refluxed 2 hrs. with BF_3-ether complex in benzene → 64 mg. 3β-acetoxy-7-oxo-$\Delta^{8,22}$-ergostadiene. H. Heusser et al., Helv. *35*, 936 (1952); 11-oxo-Δ^8-steroids, also by additional methods, s. P. Bladon, J. Elks et al., Soc. *1953*, 2921.

Aluminum chloride/sodium chloride *$AlCl_3/NaCl$*

Alkyl migration ←
s. *9*, 940

Ring closure by isomerization ○

785.

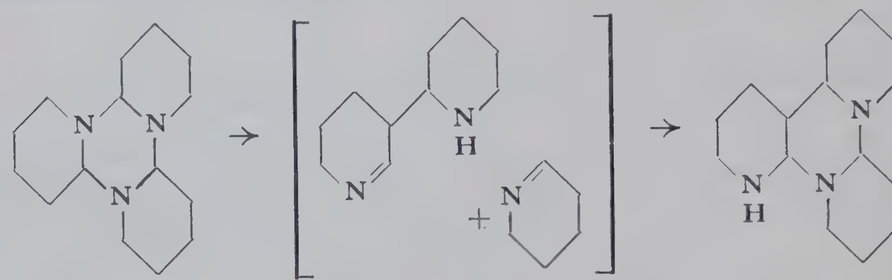


2-(s-Octahydro-9-phenanthroyl)acrylic acid added at 100° to $AlCl_3$-NaCl→1,2,3,4,5,6,7,8-octahydro-5′-keto-9,10-cyclopentenophenanthrene-3′-carboxylic acid. Y: 90%. F. isomerizations s. G. Baddeley and R. Williamson, Soc. *1953*, 2120.

Buffer pH 7.8 ←

Rearrangement of N-condensed heterocyclics ←

786.



α-Tripiperideine added rapidly with shaking at 25° to an aq. phosphate buffer soln. of pH 7.8 whereby the pH increases to 9.1, kept 5 hrs. at the same temp., then ice-cooled, satd. with K-carbonate, and extracted with ether → iso-tripiperideine. Y: 83.4-84.2%. C. Schöpf, H. Arm, and F. Braun, B. 85, 937 (1952).

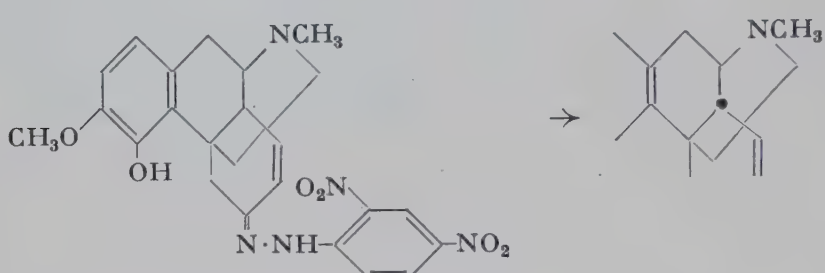
Formic acid/sulfuric acid *$HCOOH/H_2SO_4$*

s. Sulfuric acid/formic acid

Acetic acid *CH_3COOH*

cis from trans Condensed rings ←

787.



β-Thebainone-2,4-dinitrophenylhydrazone in glacial acetic acid heated 6 hrs. on a steam bath → thebainone-2,4-dinitrophenylhydrazone. Crude Y: 78%. F. methods s. M. Gates and R. Helg, Am. Soc. 75, 379 (1953).

Phosphorus pentoxide *P_2O_5*

Isotopic position isomerization ←

788. $(C_6H_5)_2\overset{\times}{C}=CHC_6H_5 \rightarrow (C_3H_5)_2C=\overset{\times}{C}HC_6H_5$

743 mg. 1,1,2-triphenylethylene-1-C^{14} refluxed 30 min. with P_2O_5 in xylene → 362 mg. 50:50 mixture of startg. m. and 1,1,2-triphenylethylene-2-C^{14}. C. J. Collins and W. A. Bonner, Am. Soc. 75, 5379 (1953).

Phosphoric acid *H_3PO_4*

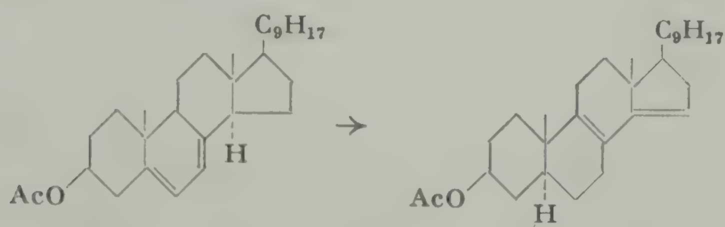
Ring closure to isocyclics ○

s. *5*, 515; s. a. H. R. Vogt and H. Schinz, Helv. *37*, 2196 (1954)

Sulfur dioxide *SO_2*

Migration of double bonds ←

789.

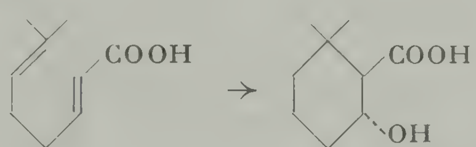


Commercial *liq.* SO_2 added to ergosteryl acetate in a tube cooled to -60^0, the tube sealed and heated 18 hrs. in a water bath → ergosteryl B_1 acetate. Y: 86%. F. e. s. A. W. D. Hudgell, J. H. Turnbull, and W. Wilson, Soc. *1954*, 814.

Sulfuric acid/formic acid *$H_2SO_4/HCOOH$*

Ring closure by isomerization with simultaneous hydration Stereospecific reactions ○

790.



A mixture of 98-100%-formic acid and concd. H_2SO_4 added to 1.1 g. 7-methyl-2,6-octadienoic acid, and allowed to stand overnight at room temp. → 0.88 g. 6,6-dimethyl-2-hydroxycyclohexanecarboxylic acid. R. Helg and H. Schinz, Helv. *35*, 2406 (1952); without hydration s. Helv. *34*, 1168 (1951); stereospecificity s. Helv. *37*, 964 (1954).

Iodine *I*

cis-trans-Rearrangement ←

s. *4*, 669; s. a. W. Oroshnik and A. D. Mebane, Am. Soc. *76*, 5719 (1954)

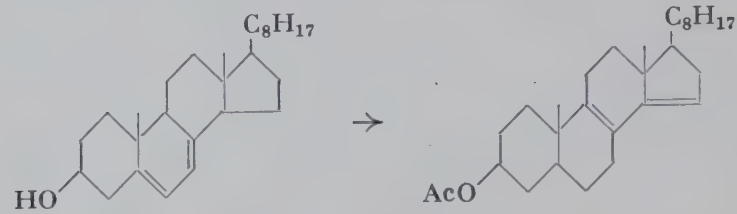
Hydrochloric acid *HCl*

Ketones from enolethers with migration of a carbon-carbon double bond ←

s. *9*, 86

←

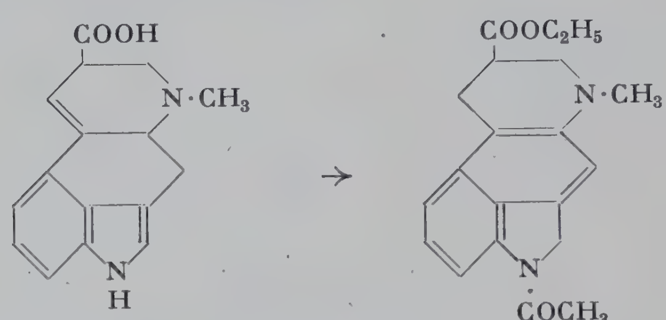
Migration of carbon-carbon double bonds and acetylation
Steroids

791. 

A soln. of crude 7-dehydrocholesterol in acetic acid-benzene containing 36%-HCl heated and the benzene allowed to evaporate, then treated slowly with a mixture prepared by adding cautiously a little 36%-HCl to acetic anhydride, refluxed 1 hr., then Na-acetate added to neutralize the mineral acid → $\Delta^{8,14}$-cholestadienyl acetate. Y: 80%. L. F. Fieser and G. Ourisson, Am. Soc. *75*, 4404 (1953).

←

Naphthalene- from indole ring by migration of carbon-carbon double bonds, with simultaneous esterification

792. 

1 g. rac. lysergic acid dissolved in alcohol which has been satd. with HCl at 0°, heated 20 min. on a steam bath in a sealed tube, and the product isolated as the 4-acetyl derivative → 0.9 g. 4-acetyl-4,5,7,8,9,10-hexahydro-7-methyl-9-carbethoxyindolo[4.3-f.g]quinoline.—At 0°, esterification takes place without rearrangement. A. Stoll and T. Petrzilka, Helv. *36*, 1125 (1953).

Oxygen/Carbon Type CC↶OC

Without additional reagents *w.a.r.*

Allylphenols from allyl ethers
Claisen rearrangement

s. *2*, 621; *4*, 671; s. a. R. Schwarz and K. Capek, M. *84*, 595 (1953)

Potassium hydroxide *KOH*

Spiroindoxyls from carbazole ring

s. *7*, 742; s. a. R. J. S. Beer et al., Soc. *1952*, 4351

Potassium hydroxide/pyridine *KOH/C_5H_5N*

Baker-Venkataraman transformation ←

s. *6*, 868; s. a. K. M. Gallagher et al., Soc. *1953*, 3770

Potassium amide *KNH_2*

Alcohols from ethers with rearrangement
Wittig rearrangement

s. *7*, 746; also isocyclic alcohols from O-heterocyclics and limitations s. J. Org. Chem. *18*, 801 (1953)

Dialkylaniline *$C_6H_5NR_2$*

Allyl phenols from allyl ethers ←
Claisen rearrangement

with diethylaniline s. *4*, 674; with dimethylaniline, also ortho-para migration, s. E. N. Marvell and R. Teranishi, Am. Soc. *76*, 6165 (1954)

Boron fluoride *BF_3*

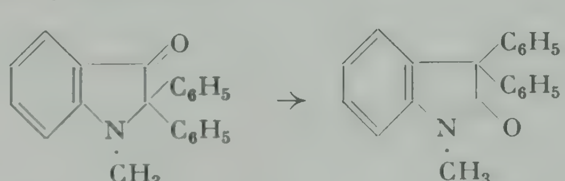
β-Ketoaldehydes from α,β-oxidoketones ←

793.

A soln. of *trans*-chalcone oxide in abs. ether treated with ethereal 45%-BF_3, refluxed 30 min., and the product isolated as the Cu-salt → Cu-salt of formyldesoxybenzoin. Y: ca. 100%. F. e. s. H. O. House, Am. Soc. *76*, 1235 (1954).

ψ-Oxindoles from ψ-indoxyls ←

794.

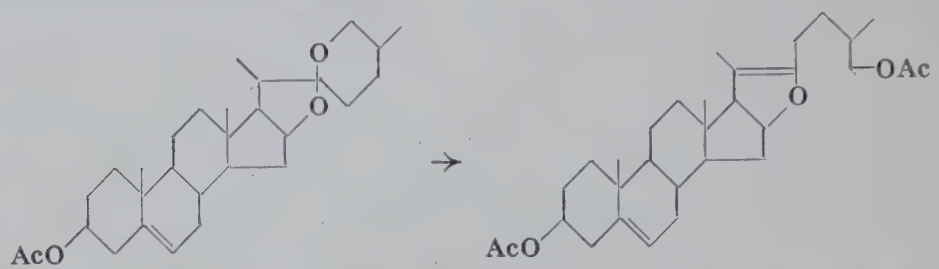


0.5 g. 2,2-diphenyl-1-methyl-ψ-indoxyl refluxed 10 min. with BF_3-etherate → 0.44 g. 3,3-diphenyl-1-methyl-ψ-oxindole. F. e. s. B. Witkop and A. Ek, Am. Soc. *73*, 5664 (1951).

Aluminum chloride *AlCl₃*

Furostenes from spirostanes

795.

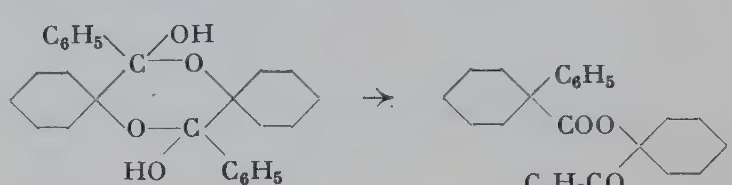


A soln. of 20 g. 22-iso-5-spirosten-3β-ol acetate in acetic anhydride treated with $AlCl_3$, and refluxed 4 hrs. → 17 g. crude 5,20(22)-furostadiene-3β,26-diol diacetate.—Catalysts of the Lewis acid type permit this isomerization at the boiling point of acetic anhydride rather than at 200° (cf. Synth. Meth. *7*, 749). D. H. Gould, H. Staeudle, and E. B. Hershberg, Am. Soc. *74*, 3685 (1952).

Formic acid *HCOOH*

α-Acoxyketones from p-dioxanes

796.

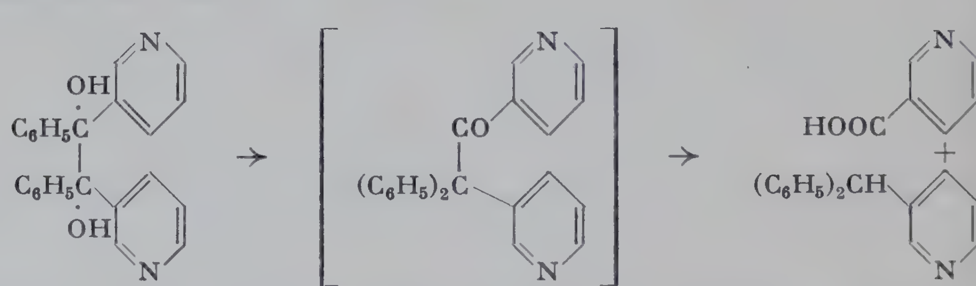


5 g. 1-hydroxycyclohexyl phenyl ketone dimer (prepn. s. 309) refluxed 12 hrs. with anhydrous formic acid → 3.3 g. 1-benzoylcyclohexyl 1-phenylcyclohexanecarboxylate. I. Elphimoff-Felkin and B. Tchoubar, Bl. *1952*, 551.

Acetyl chloride *CH_3COCl*

Pinacol rearrangement with subsequent hydrolytic cleavage of the carbon chain ←

797.



A mixture of dry benzene, glacial acetic acid, and acetyl chloride added to 1,2-di-(3-pyridyl)-1,2-diphenylethane-1,2-diol (prepn. s. 731), refluxed 44 hrs. at 90°, the bulk of the volatile material removed in vacuo at 90°,

the residue freed of the last of the acetic acid by storage in a vacuum desiccator over KOH, and the resulting pinacolone residue refluxed with a soln. of KOH in methanol → crude 3-pyridyldiphenylmethane (Y: 62%) and nicotinic acid (Y: 79% by potentiometric titration). F. e. s. M. R. Kegelman and E. V. Brown, Am. Soc. 75, 4649, 5961 (1953).

Sulfuric acid *H_2SO_4*

Phenol acetates from dienones ←

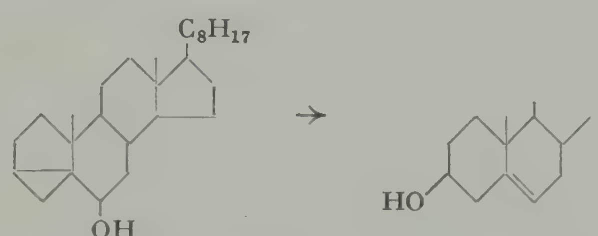
s. *3*, 597; *6*, 720; s. a. C. Djerassi and T. T. Grossnickle, Am. Soc. *76*, 1741 (1954); unusual dienone-phenol rearrangement s. E. N. Marvell and A. O. Geiszler, Am. Soc. *74*, 1259 (1952)

Ring expansion

s. *6*, 720; s. a. R. H. Burnell and W. J. Taylor, Soc. *1954*, 3486

Steroids from 3,5-cyclosteroids C

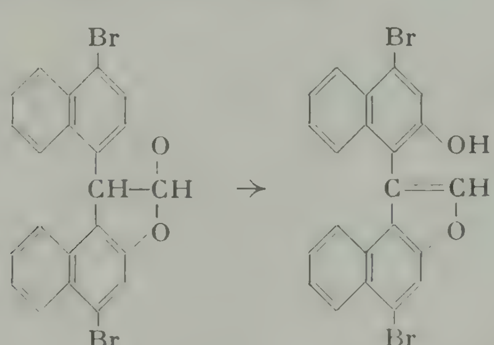
98.



Concd. H_2SO_4 added to a soln. of epi-i-cholesterol in glacial acetic acid, warmed 1 hr. at 50-55°, poured into water, extracted with ether, and the resulting crude acetate hydrolyzed by treating with ethanolic 10%-KOH at 45° for 1 hr. → 3β-cholesterol. Y: ca. 98%. F. e. s. A. F. Wagner, N. E. Wolff, and E. S. Wallis, J. Org. Chem. *17*, 529 (1952).

Hydroxyenolethers from inner acetals

99.



5.2 g. inner acetal of bis-(4-bromo-2-hydroxy-1-naphthyl)acetaldehyde boiled 2 hrs. in glacial acetic acid containing H_2SO_4 and a little water → 5.2 g. 5-bromo-1-(4-bromo-2-hydroxy-1-naphthyl)naphtho[2.1-b]-furan. F. e. s. O. Dischendorfer and H. Lapaine, M. *82*, 397 (1951).

Ring expansion ←
by pinacol rearrangement

s. 7, 753; also different product with $ZnCl_2$-acetic anhydride s. R. E. and G. G. Lyle, Am. Soc. 76, 3536 (1954)

Hydrochloric acid *HCl*

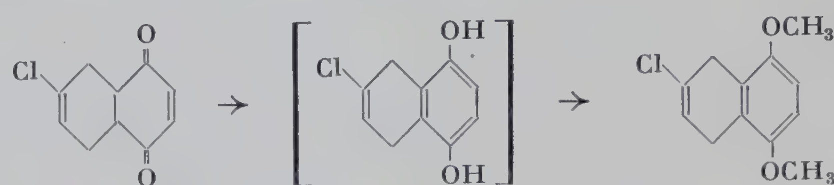
Anionotropic rearrangement ←

s. 8, 765; in side-chains of heterocyclics s. Soc. 1952, 4155, 4158

Hydrobromic acid *HBr*

Aromatization by enolization ←
Ethers

800.



5 drops of a soln. of HBr in glacial acetic acid added with stirring in a N_2-stream to a soln. of 6-chloro-5,8,4a,8a-tetrahydro-1,4-naphthoquinone in benzene, refluxed 15 min., treated with a soln. of Na in methanol under N_2, then cooled and treated with dimethyl sulfate and more Na-methoxide soln., stirred 2 hrs. at room temp. → 2-chloro-5,8-dimethoxy-1,4-dihydronaphthalene. Y: 80%. C. A. Grob and W. Jundt, Helv. 35, 2111 (1952).

Nitrogen/Carbon Type CC↶NC

Lithium methylanilide *$(C_6H_5)(CH_3)N\cdot Li$*

Cyclic iminonitriles from dinitriles ○
Ziegler cyclization

s. 5, 525; N-heterocyclics from cyanamides s. H.-J. Nitzschke and G. Faerber, B. 87, 1635 (1954)

Sodium amide *$NaNH_2$*

Migration into the ring ←

o-Methylaryl compounds s. 8, 769; s. a. Org. Synth. 34, 61 (1954); also other alkylaryl compounds s. Am. Soc. 76, 1264 (1954)

Zinc *Zn*

Nitriles from formamides via isonitriles NHCHO → CN

01. 

2-Methyl-6-*tert*-butylformanilide refluxed 1 hr. with excess Zn-dust → 2-methyl-6-*tert*-butylbenzonitrile. Y: 52%. P. J. C. Fierens and J. van Rysselberge, Bull. soc. chim. Belges *61*, 215 (1952).

Carbon/Carbon Type CC⤺CC

Sodium nitrite *$NaNO_2$*

Cyclic alcohols from aminomethylcycloalkanes
Demyanov ring expansion ←

s. *1*, 540; s. a. P. A. S. Smith, D. R. Baer, and S. N. Ege, Am Soc. *76*, 4564 (1954)

Cyclic ketones from cyclic aminomethylalcohols
Tiffeneau ring expansion

s. *1*, 539, 541; s. a. F. F. Blicke, N. J. Doorenbos, and R. H. Cox, Am. Soc. *74*, 2924 (1952); H. J. Dauben et al., Org. Synth. *34*, 19 (1954)

Exchange

Hydrogen ▴ CC⇅H

Without additional reagents *w.a.r.*

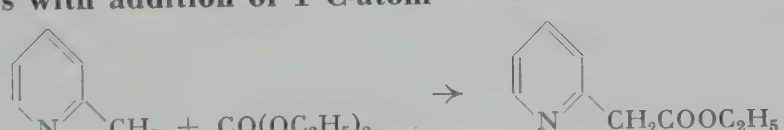
Cyanogenation H → CN

02. $C_6H_6 + (CN)_2 \rightarrow C_6H_5CN + HCN$

Benzene allowed to react with a twofold excess of cyanogen in a vertical silica tube at 745° and 2-3 sec. contact time → benzonitrile. Y: 42%; conversion ca. 46%. F. e. s. G. J. Janz, Am. Soc. *74*, 4529 (1952).

Phenyllithium *C_6H_5Li*

Carboxylic acid esters from hydrocarbons H → COOR
Synthesis with addition of 1 C-atom

03. 

2-Picolyllithium prepared from 2-picoline and phenyllithium (from Li-ribbon and bromobenzene) in ether added with rapid stirring during

5 hrs. to an ice-salt cooled soln. of diethyl carbonate in ether, heated to reflux, then poured onto ice → ethyl 2-pyridylacetate. Y: 44.5%. N. N. Goldberg, B. M. Perfetti, and R. Levine, Am. Soc. 75, 3843 (1953).

Cuprous chloride *CuCl*

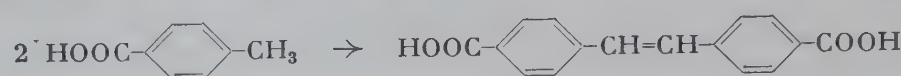
Diacetylene derivatives by coupling of acetylene derivatives $RH + HR' \rightarrow R \cdot R'$

s. 4, 687; s. a. B. L. Shaw and M. Whiting, Soc. 1954, 3217

Sulfur *S*

Ethylene derivatives by dimerization $2\ RCH_3 \rightarrow RCH{:}CHR$

804.



A mixture of p-toluic acid and S heated 2 hrs. at 271° → 4,4′-stilbenedicarboxylic acid. Y: 57.3% based on startg. m. converted. W. G. Toland. Jr., J. B. Wilkes, and F. J. Brutschy, Am. Soc. 75, 2263 (1953); 76, 307 (1954).

Persulfate $S_2O_8^{--}$

Oxidative dimerization of aliphatic nitro compounds $2\ RH \rightarrow R \cdot R$

805.

$$2\ (CH_3)_2CHNO_2 \rightarrow \begin{array}{c}(CH_3)_2C \cdot NO_2 \\ | \\ (CH_3)_2C \cdot NO_2\end{array}$$

A mixture of NH_4-persulfate and Na-acetate in water added at 0-5° to a soln. of 2-nitropropane in 10%-NaOH, and the product isolated after 6 hrs. → 2,3-dimethyl-2,3-dinitrobutane. Y: 53-62%. F. e. s. H. Shechter and R. B. Kaplan, Am. Soc. 75, 3980 (1953).

Via intermediates *v.i.*

α,β-Ethylenenitriles from ethylene derivatives $H \rightarrow CN$

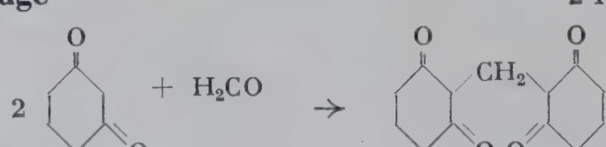
s. 9, 899

Oxygen ↓ CC⇅O

Without additional reagents *w.a.r.*

Methylene bridge $2\ RH \rightarrow R \cdot CH_2 \cdot R$

806.



A 40%-formalin soln. added to an aq. soln. of 1,3-cyclohexanedione, cautiously heated until the soln. becomes turbid, heating stopped, and

the mixture allowed to stand 12 hrs. at room temp. → methylenebisdihydroresorcinol (startg. m. f. 228). Y: ca. 100%. H. Stetter and W. Dierichs, B. *85*, 290 (1952).

Mannich reaction
Aminomethylation H → $CH_2N<$

with N-heterocyclics

s. *3*, 608; s. a. J. Thesing and H. Mayer, B. *87*, 1084 (1954); J. H. Burckhalter, W. H. Edgerton, and J. H. Durden, Jr., Am. Soc. *76*, 6089 (1954)

Salts of aci-α,γ-dinitroglutaric acid esters from aldehydes and nitroacetic acid ester ←

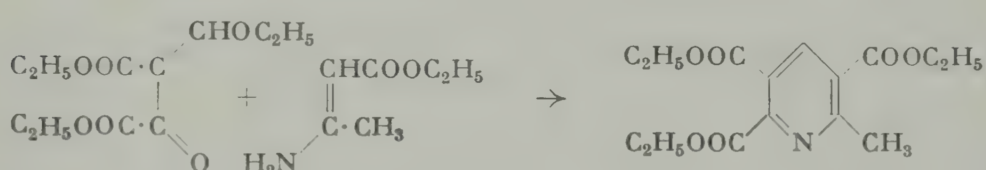
s. *9*, 856

2,3-Pyrrolidiones ○

s. *3*. 611; s. a. W. Ried and H. Gutjahr, B. *86*, 1096 (1953)

Pyridine ring from enamines

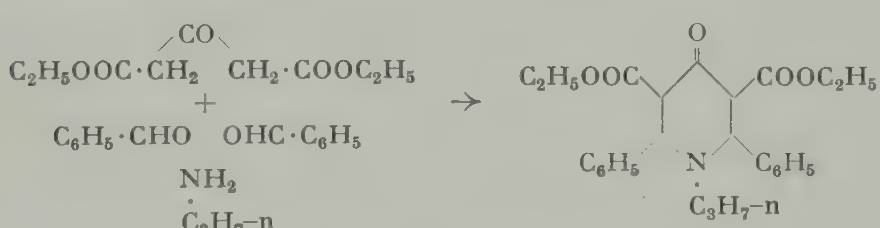
07.



Ethyl β-aminocrotonate added to a soln. of diethyl ethoxymethyleneoxalacetate in anhydrous ether → triethyl 6-methyl-2,3,5-pyridinetricarboxylate. Y: 86%. F. e. s. E. M. Bottorff et al., Am. Soc. *73*. 4380 (1951); s. a. R. G. Jones, Am. Soc. *73*, 5610 (1951).

4-Piperidones

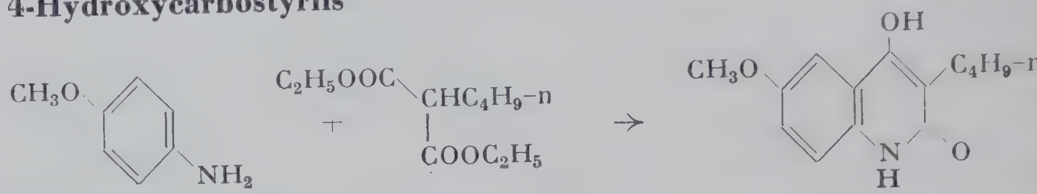
08.



n-Propylamine added dropwise to a mixture of diethyl acetonedicarboxylate and benzaldehyde → diethyl 1-propyl-2,6-diphenyl-4-piperidone-3,5-dicarboxylate. Y: 82.5%. F. e. s. P. Soni and G. S. Sidhu, J. Indian Chem. Soc. *28*, 405 (1951).

4-Hydroxycarbostyrils

809.



Equimolecular amounts of diethyl n-butylmalonate and p-anisidine refluxed 8 hrs. with Dowtherm A → 3-n-butyl-4-hydroxy-6-methoxycarbostyril. Y: 91%. R. R. Holmes et al., Am. Soc. *76*, 2400 (1954); method s. R. H. Baker, G. R. Lapin, and B. Riegel, Am. Soc. *68*, 1284 (1946).

Lithium *Li*

Ketones form carboxylic acids COOH → COR

810.

Ethereal methyl-Li, prepared from methyl iodide and Li, added dropwise during 3.5 hrs. with vigorous stirring at 15° under N_2 to 1-hydroxycyclohexane-1-carboxylic acid in ether → 1-acetylcyclohexanol. Y: 73%.—By other procedures, a partial conversion of the carboxyl group to a tert. alcohol occurs. J. D. Billimoria and N. F. Maclagan, Soc. *1951*, 3067; f. e. s. C. Tegner, Acta Chem. Scand. *6*, 782 (1952); H. Kappeler et al., Helv. *37*, 957 (1954).

Sodium hydride *NaH*

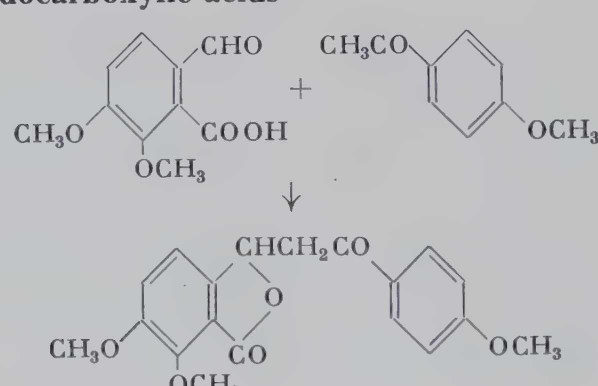
β-Ketocarboxylic acid esters $COCH_2COOR$
from carboxylic acid esters
Mixed ester condensation

s. *6*, 738; *7*, 434; fluorine-containing compounds s. E. T. McBee et al., Am. Soc. *75*, 3152 (1953)

Sodium hydroxide *NaOH*

Subst. phthalides ←
from o-aldehydocarboxylic acids

811.



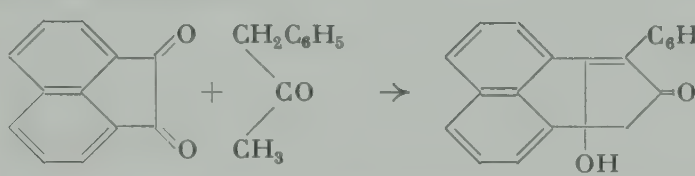
Methanol added to a suspension of 16 g. p-methoxyacetophenone and 21 g. opianic acid in 10%-NaOH until a homogeneous soln. is obtained. then kept 24 hrs. at room temp. → 29.5 g. 6,7-dimethoxy-3-(4-methoxyphenacyl)phthalide. F. e. s. A. S. Bailey and R. S. Staunton, Soc. *1952*, 2153.

Potassium hydroxide *KOH*

α,β-Ethylenenitriles from aldehydes CHO → CH:C·CN

s. *7*, 271; also with Na-ethoxide, pyridine, and other condensing agents s. A. Schonne, E. Braye, and A. Bruylants, Bl. Soc. chim. Belg. *62*, 155 (1953)

Condensed cyclohexenolones ○

812. 

Acenaphthenequinone and benzyl methyl ketone in methanolic KOH stirred 3 hrs. at room temp. → condensed cyclohexenolone. Y: 78%. F. e. s. C. F. H. Allen and J. A. VanAllan, J. Org. Chem. *17*, 845 (1952).

Sodium/alcohol *NaOR*

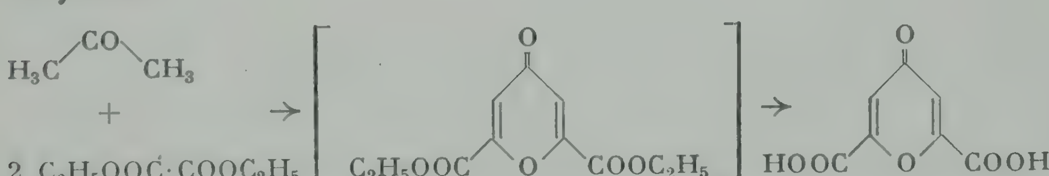
Oxalic ester synthesis H → COCOOR

s. *3*, 620; 5-tetrazolylpyruvates s. C. R. Jacobsen and E. D. Amstutz, J. Org. Chem. *18*, 1183 (1953)
s. *4*, 703; s. a. Org. Synth. *34*, 13 (1954)

α-Cyanoketones from nitriles CHCN → C(CN)COR

s. *2*, 645; s. a. W. Logemann, L. Almirante, and L. Caprio, B. *87*, 435 (1954)

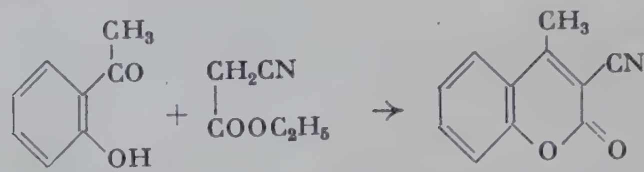
4-Pyrones ○

813. 

A soln. of Na in abs. ethanol added to a mixture of acetone and ethyl oxalate. when the soln. becomes turbid more ethyl oxalate and Na-ethoxide soln. added, the crude chelidonic ester isolated after ca. 10 min. and hydrolyzed by heating 20 hrs. with concd. HCl on a steam bath → chelidonic acid. Y: 72%. R. F. Toomey and E. R. Riegel, J. Org. Chem. *17*, 1492 (1952).

Coumarin ring

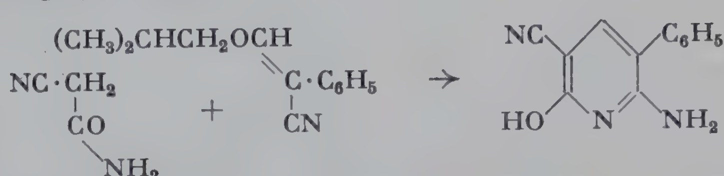
814.



A mixture of o-hydroxyacetophenone, ethyl cyanoacetate, and some Na-ethoxide in abs. ethanol refluxed 2 hrs. after the appearance of needle-shaped crystals → 3-cyano-4-methylcoumarin (startg. m. f. 279). Y: 79%.—Na-ethoxide catalyzes the aldol condensation better than pyridine and piperidine. C. H. Schroeder and K. P. Link, Am. Soc. *75*, 1886 (1953).

Pyridine ring synthesis

815.



A mixture of isobutoxymethylenephenylacetonitrile, cyanoacetamide. and a soln. of Na in abs. ethanol refluxed 6 hrs. in a slow stream of N_2 → 2-amino-5-cyano-6-hydroxy-3-phenylpyridine. Y: 81%. F. e. s. B. H. Chase and J. Walker, Soc. *1953*, 3548.

Sodium methoxide *$NaOCH_3$*

β-Ketoacetals from ketones via α-hydroxymethyleneketones $COCH_3 \rightarrow COCH_2CH(OR)_2$

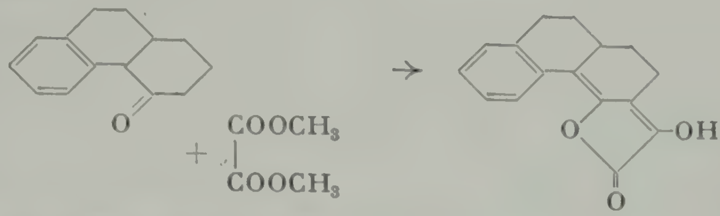
816.

$$(CH_3)_2CHCH_2COCH_3 + HCOOCH_3 + NaOCH_3$$
$$\downarrow$$
$$[(CH_3)_2CHCH_2COCH{=}CHONa] + 2\ CH_3OH$$
$$\downarrow$$
$$(CH_3)_2CHCH_2COCH_2CH(OCH_3)_2$$

A mixture of isobutyl methyl ketone and methyl formate added with stirring to a slurry of Na-methoxide in abs. ether at a rate to maintain gentle reflux, stirring continued 1 hr., most of the ether removed without stirring under reduced pressure, methanol added to the solid Na-hydroxymethyleneketone followed by a soln. of anhydrous HCl in methanol, stirring continued 1-2 hrs. at 20°, and made just alkaline to litmus with satd. methanolic KOH → 1,1-dimethoxy-5-methyl-3-hexanone. Y: 69.4%. F. e. s. E. E. Royals and K. C. Brannock, Am. Soc. *75*, 2050 (1953).

Dienollactones

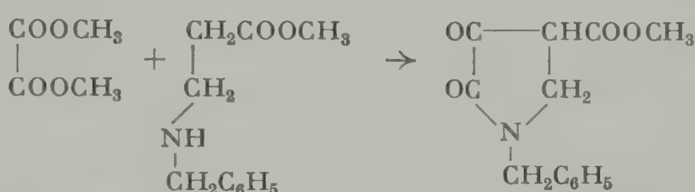
817.



A mixture of methyl oxalate, Na-methoxide, and benzene refluxed 10 min. under N_2, a soln. of 2 g. *trans*-1,2,3,4,9,10,11,12-octahydro-4-keto-phenanthrene in benzene added, stirred 5 hrs. at room temp. under N_2, the crude solid Na-salt thus obtained suspended in dioxane, and HCl added to just neutral reaction → 1.8 g. lactone. F. e. s. D. Ginsburg and R. Pappo, Soc. *1953*, 1524.

2,3-Pyrrolidiones

818.



Methyl oxalate followed by a soln. of methyl β-benzylaminopropionate in anhydrous ether added to a well-stirred suspension of Na-methoxide in ether, and refluxed 0.5 hr. with stirring → 4-carbomethoxy-1-benzyl-2,3-dioxopyrrolidine. Y: 75%. F. e. s. P. L. Southwick and R. T. Crouch, Am. Soc. 75, 3413 (1953).

Potassium tert-butoxide *KOR*

Subst. unsatd. succinic acid monoesters ←
Stobbe condensation

s. *2*, 647; s. a. G. Büchi and J. J. Pappas, Am. Soc. *76*, 2963 (1954); G. N. Walker, Am. Soc. *75*, 3387 (1953)

n-Butyllithium C_4H_9Li

Synthesis of sym. ketones $2\ RH + CO_2 \rightarrow R_2CO$
with carbon dioxide
Metalation of thiophenes

819.

Thiophene allowed to react with n-butyl-Li in ether under N_2, gently refluxed for an additional 15 min., then CO_2 in place of N_2 bubbled into the soln. for 10 hrs. until the test for organo-Li compound is negative → di-2-thienyl ketone. Y: 67%. N. M. Löfgren and C. Tegner, Acta Chem. Scand. *6*, 1020 (1952).

Sodium/liq. ammonia *Na/NH_3*

Synthesis of acetylene derivatives CH → CR

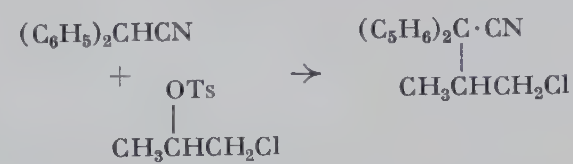
820. $HC{\equiv}C\cdot C{\equiv}CNa + (C_2H_5O)_2SO_2 \rightarrow HC{\equiv}C\cdot C{\equiv}C\cdot C_2H_5$

Mono-Na-diacetylide prepared from diacetylene and Na in liq. NH_3 allowed to react with diethyl sulfate → 1,3-hexadiyne. Y: almost 100%. F. e. s. T. Herbertz, B. *85*, 475 (1952).

Sodium amide *$NaNH_2$*

Alkylation of nitriles with p-toluenesulfonic acid esters

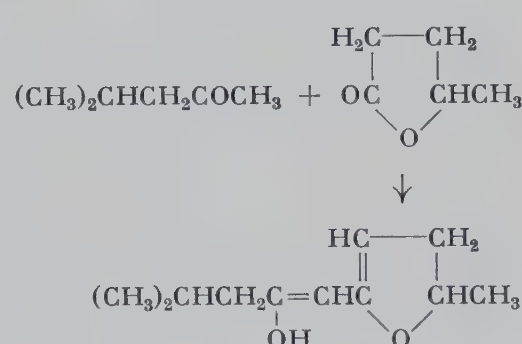
821.



A soln. of diphenylacetonitrile in dry toluene added to a slurry of $NaNH_2$ in toluene, heated with stirring to 106° under N_2, heating and stirring continued until 95% or more of the theoretical amount of NH_3 is evolved, cooled to 65°, 1-chloro-2-propyl p-toluenesulfonate added slowly with stirring below 80°, and refluxed 18 hrs. with stirring → 4-chloro-2,2-diphenyl-3-methylbutanenitrile. Y: 65%.—The sec. tosyl ester group is more reactive than the prim. chlorine atom. M. Sletzinger, E. M. Chamberlin, and M. Tishler, Am. Soc. *74*, 5619 (1952).

Synthesis of dihydrofurans from γ-lactones ←

822.

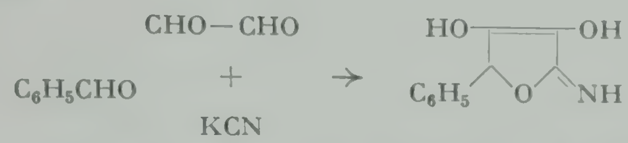


Isobutyl methyl ketone added dropwise during 20-30 min. to $NaNH_2$ in ether, agitated for an additional 10 min., γ-valerolactone in anhydrous ether added during 30 min., and refluxed 8 hrs. on a water bath → 5-methyl-2-(2′-hydroxy-4′-methyl-1′-pentenyl)-4,5-dihydrofuran. Y: 59.3%. F. e., with lower yields, s. G. W. Cannon, J. J. Casler, Jr., and W. A. Gaines, J. Org. Chem. *17*, 1245 (1952).

Sodium carbonate Na_2CO_3

3,4-Dihydroxy-2-imino-2,5-dihydrofurans from aldehydes

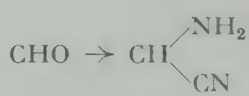
823.



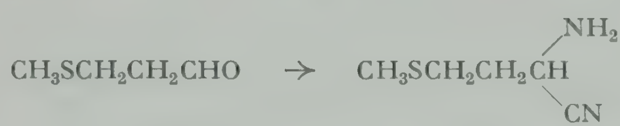
Glyoxal hydrogen sulfite dihydrate and a soln. of benzaldehyde in dioxane added with stirring in a N_2-stream to a soln. of KCN in aq. 2 *N* Na-carbonate, after 30 min. adjusted with glacial acetic acid to pH 6, and stirring continued for 3 hrs. → 4-phenyl-2-hydroxytetronimide. Y: 93%. F. e. s. H. Dahn et al., Helv. *37*, 1309 (1954).

Sodium cyanide *NaCN*

α-prim-Aminonitriles from aldehydes
Synthesis with addition of 1 C-atom



824.

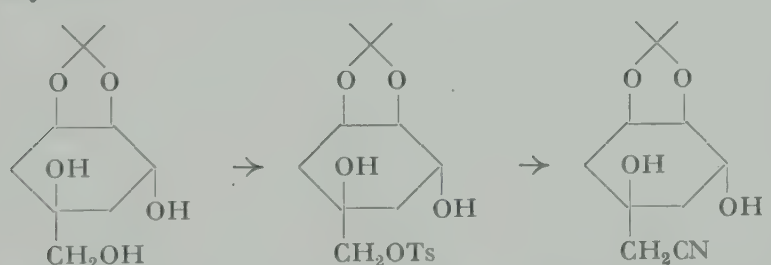


β-Methylthiopropionaldehyde added dropwise with stirring during 30 min. at 15-20° to a mixture of NH_4Cl, NaCN, concd. aq. NH_3, and alcohol satd. with NH_3, stirring continued overnight → α-amino-γ-methylthiobutyronitrile. Y: 95.5%. D. O. Holland and J. H. C. Nayler, Soc. *1952*, 3403.

Potassium cyanide *KCN*

Nitriles from p-toluenesulfonic acid esters ←
Partial tosylation

825.



A soln. of acetone quinalcohol in abs. pyridine mixed at −40° in a closed apparatus (s. original paper) with a soln. of p-toluenesulfonyl chloride in chloroform, and allowed to stand 3 days at −20° → crude monotosyl derivative (Y: ca. 85%) dissolved in alcohol, treated with KCN, and kept 16 hrs. at 40° with occasional shaking → isopropylidene-homoquinonitrile (Y: ca. 75%). Overall Y: 64%. F. e. for the second step s. R. Grewe and E. Nolte, A. *575*, 1 (1952).

α-Aminonitriles from oxo compounds CO → C(CN)N<

s. *6*, 752; *7*, 777; bis-(α-aminonitriles) s. H. Zahn and H. Wilhelm, A. *579*, 1 (1953)

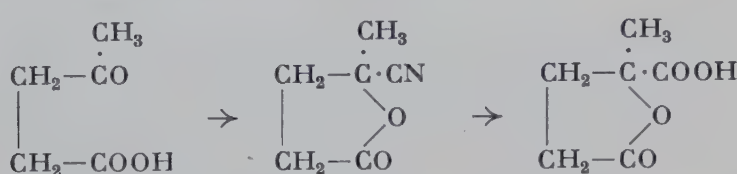
Hydantoins from oxo compounds ○

s. *1*, 568; 5-pyridylhydantoins s. H. R. Henze and M. B. Knowles, J. Org. Chem. *19*, 1127 (1954)

Potassium cyanide/hydrochloric acid *KCN/HCl*

Carboxylactones from ketocarboxylic acids via cyanolactones ○

826.

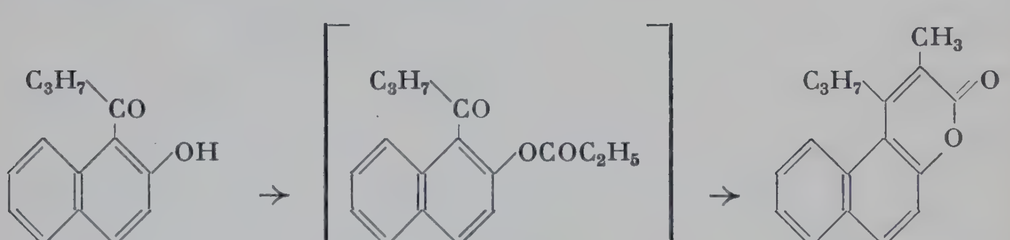


Cold aq. levulinic acid added with stirring during 30 min. to cold aq. KCN, stirred 24 hrs. at 0°, acidified by slow addition of concd. HCl, stirred at 0° for another 24 hrs., then heated 10 min. at 100° → DL-γ-cyano-γ-valerolactone (Y: 55.8%) refluxed 21 hrs. with 20.8%-HCl → DL-γ-carboxy-γ-valerolactone (Y: 94%). F. e. s. R. Adams and F. Hauserman, Am. Soc. *74*, 694 (1952).

Sodium salt *Na⁺*

Kostanecki-Robinson reaction
Coumarin ring from o-hydroxyketones

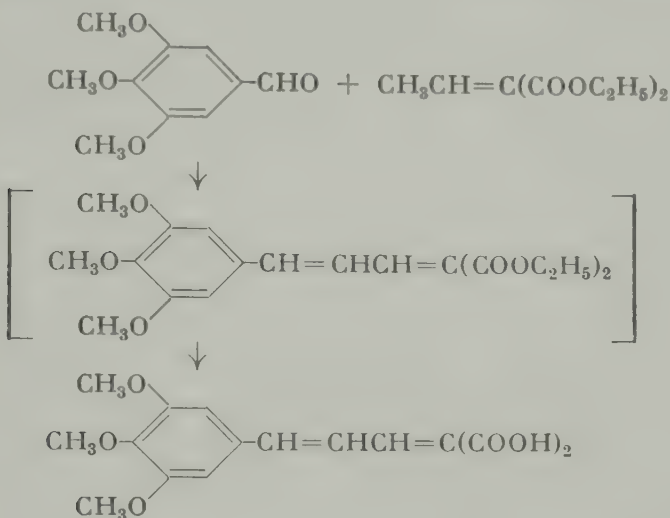
827.



A mixture of 1 mole 1-butyryl-2-naphthol, 6.5 moles propionic anhydride, and 4.5 moles Na-propionate heated 6 hrs. in an oil bath at 160°, cooled, then boiled 2 hrs. with water to decompose the excess acid anhydride → 3-methyl-4-propylnaphthocoumarin. Y: 88%.—Depending on the startg. m., coumarins or chromones, or mixtures thereof are obtained. F. e. s. A. B. Sen and T. N. Kakaji, J. Indian Chem. Soc. *29*, 127, 950 (1952).

Triton B ←

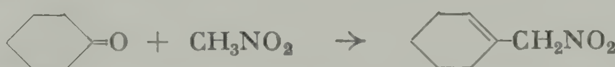
Cinnamylidenemalonic acids from aldehydes CHO → CH: CHCH: C(COOH)$_2$

828. 

Methanolic 35%-benzyltrimethylammonium hydroxide added to a mixture of 3,4,5-trimethoxybenzaldehyde, ethyl ethylidenemalonate, and abs. ethanol, allowed to stand 24-48 hrs. at room temp., and the ester hydrolyzed by addition of water and refluxing 30-60 min. → 3,4,5-trimethoxycinnamylidenemalonic acid. Y: 86%. F. e. s. P. D. Gardner et al., Am. Soc. *74*, 5527 (1952).

Methylamine *CH_3NH_2*

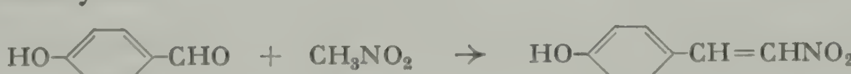
β,γ-Nitroethylene derivatives from ketones ←

829. 

Anhydrous liq. methylamine added at 5° to a mixture of cyclohexanone and nitromethane, and kept 17 days at 8-10° → 1-nitromethyl-1-cyclohexene. Y: 48%. With piperidine, only 26% yield was obtained. F. e. s. D. V. Nightingale, F. B. Erickson, and J. M. Shackelford, J. Org. Chem. *17*, 1005 (1952).

Aniline *$C_6H_5NH_2$*

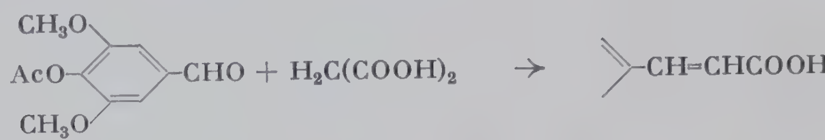
α,β-Nitroethylene derivatives from aldehydes CHO → CH: C·NO$_2$

830. 

A mixture of 4-hydroxybenzaldehyde, nitromethane, and aniline heated 1 hr. on a water bath → 4-hydroxy-β-nitrostyrene. Y: 79%. F. e. and methods s. O. Schales and H. A. Graefe, Am. Soc. *74*, 4486 (1952).

Aniline, pyridine *$C_6H_5NH_2$, C_5H_5N*

α,β-Ethylenecarboxylic acids from aldehydes Synthesis with addition of 2 C-atoms CHO → CH:CHCOOH

831. 

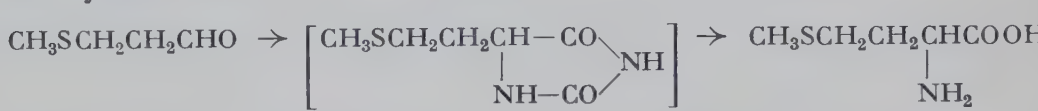
Several drops of aniline added to a soln. of acetylsyringaldehyde and malonic acid in warm pyridine, kept 4 hrs. at 20° and 6 hrs. at 50° → acetylsinapic acid. Y: 84%. K. Freudenberg and H. H. Hübner, B. *85*, 1181 (1952).

Triethylamine *$(C_2H_5)_3N$*

Thiomethylation H → CH_2SR

s. *9*, 844

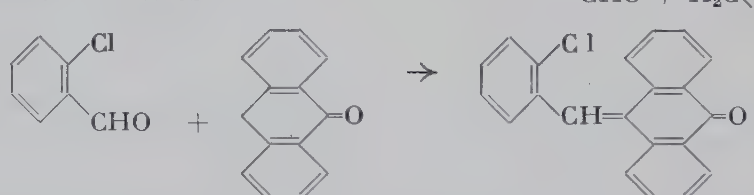
α-Aminocarboxylic acids from oxo compounds via hydantoins ←

832. 

Triethylamine followed by β-methylthiopropionaldehyde added with stirring to a mixture of NaCN and $(NH_4)_2CO_3$ in 50% aq. alcohol. after 1 hour's stirring kept overnight, dil. with alcohol, after ca. 15 min. the precipitated Na-carbonate removed and washed with alcohol, water and $Ba(OH_2)$ added to the aq. alc. filtrate, boiled to remove alcohol and triethylamine, then refluxed 36 hrs. → methionine. Y: 79-82%. Also isolation of te intermediate s. D. O. Holland and J. H. C. Nayler, Soc. *1952*, 3403.

Piperidine *$C_5H_{11}N$*

10-Arylideneanthrones CHO + $H_2C\langle$ → $CH:C\langle$

833. 

A mixture of anthrone, o-chlorobenzaldehyde, and several drops of piperidine heated 10 min. at 150-160° → 10-(o-chlorobenzylidene)-anthrone. Y: ca. 100%. E. D. Bergmann, Y. Hirshberg, and D. Lavie. Bl. *1952*, 268.

α,β-Ethylene-α-cyanocarboxylic acid esters from aldehydes CHO → CH:C(CN)COOR

s. 7, 781; s. a. J. Harley-Mason and A. H. Jackson, Soc. *1954*, 1165

β-Subst. glutaric acids from aldehydes via arylmethylene-bis-acetoacetates ←

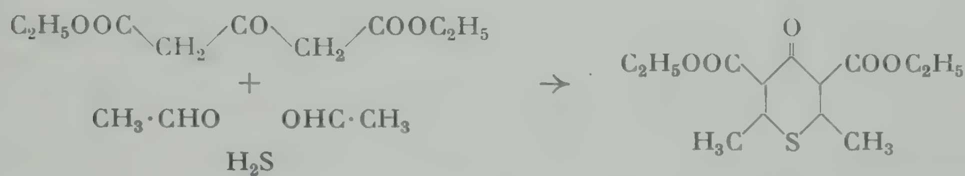
s. *6*, 759; s. a. Am. Soc. *76*, 2731 (1954)

Eneheterocyclics ←

s. *9*, 336

Tetrahydrothio-4-pyrones ○

834.

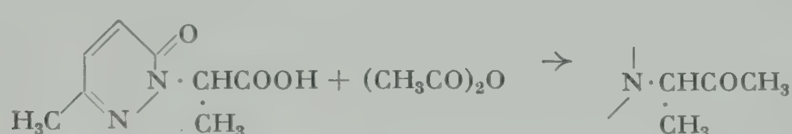


1 mole piperidine added dropwise at –15 to –10° to a soln. of diethyl acetonedicarboxylate in ethanol, then acetaldehyde in ethanol added, and H_2S introduced at the same temp. for 25 min. → 2,6-dimethyl-3,5-dicarbethoxytetrahydrothio-4-pyrone. Y: 36.7%. V. Horák and M. Černý. Collection Czechoslov. Chem. Communs. *18*, 379 (1953).

Pyridine *C_5H_5N*

Ketones from carboxylic acids COOH → COR

835.



A mixture of α-2-(6-methyl-3-pyridazonyl)propionic acid, acetic anhydride, and pyridine refluxed 2 hrs., during which time CO_2 is freely evolved → methyl 1-[2-(6-methyl-3-pyridazonyl)]ethyl ketone. Y: 78%. F. e. s. J. A. King and F. H. McMillan, Am. Soc. *74*, 3222 (1952).

Cuprous cyanide *CuCN*

Nitriles from alcohols OH → CN

s. *7*, 787; s. a. Am. Soc. *74*, 2987 (1952)

Zinc *Zn*

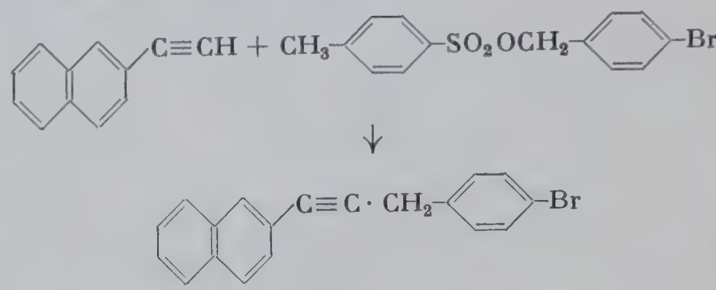
Knorr pyrrole synthesis ○

s. *1*, 587; also with benzyl instead of ethyl acetoacetate s. S. F. MacDonald, Soc. *1952*, 4176

Ethylmagnesium bromide *C_2H_5MgBr*

Synthesis of hydrocarbons from p-toluenesulfonic acid esters RH + TsOR′ → R·R′

836.



The Grignard reagent obtained by refluxing β-naphthylacetylene with an equivalent amount of ethyl-MgBr in ether-benzene for 7 hrs. added dropwise with stirring to a refluxing soln. of p-bromobenzyl p-toluenesulfonate in benzene-ether, and refluxed 8 hrs. with stirring → 1-(p-bromophenyl)-3-(β-naphthyl)-2-propyne. Crude Y: 66%. T. L. Jacobs and S. Singer, J. Org. Chem. *17*, 475 (1952).

Acetals from orthoformic acid esters Synthesis with addition of 1 C-atom CH → C·CH(OR)$_2$

837.

$$C_2H_5\cdot C{\equiv}C\cdot CH_2CH_2\cdot C{\equiv}CH + HC(OC_2H_5)_3$$
$$\downarrow$$
$$C_2H_5\cdot C{\equiv}C\cdot CH_2CH_2\cdot C{\equiv}C\cdot CH(OC_2H_5)_2$$

1,5-Octadiyne in ether added during 5 min. to an ethereal soln. of ethyl-MgBr, refluxed 2 hrs. with stirring under N_2, ethyl orthoformate added, heating under N_2 continued for 6 hrs., the ether distilled off, and the residue heated 1 hr. on a steam bath → 2,6-nonadiynal diethyl acetal. Y: 81%. F. Sondheimer, Am. Soc. *74*, 4040 (1952).

Dialkylaminomagnesium bromide *R_2NMgBr*

β-Ketocarboxylic acid esters from carboxylic acid esters COCHRCOOR′

with diethylamino-magnesium bromide s. *3*, 638; with diisopropylaminomagnesium bromide s. L. H. Sommer et al., Am. Soc. *75*, 2932 (1953)

Boron fluoride *BF_3*

Ketones from carboxylic acid anhydrides CO·O·OC → COR

s. *4*, 725; s. a. G. Tsatsas and J. Hoch, C. r. *236*, 494 (1953)

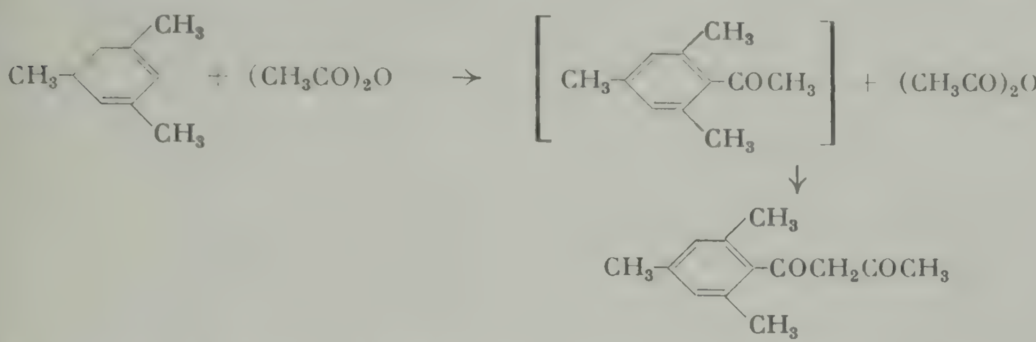
β-Diketones from carboxylic acid anhydrides ·COCH$_2$CO·

s. *1*, 579; improved procedures s. R. M. Manyik et al., Am. Soc. *75*, 5030 (1953)

Acetoacetylation

$H \rightarrow COCH_2COCH_3$

838.



A mixture of mesitylene and acetic anhydride satd. with BF_3 at 0-10° in 2-3 hrs., stirring continued to make a total reaction time of 4 hrs. → mesitoylacetone. Y: 57%. F. e. s. H. G. Walker, Jr., J. J. Sanderson, and C. R. Hauser, Am. Soc. *75*, 4109 (1953).

Aluminum chloride *$AlCl_3$*

Synthesis of hydrocarbons from p-toluenesulfonic acid esters $ArH + TsOR \rightarrow ArR$

839. $n\text{-}C_{18}H_{37}OTs + C_6H_6 \rightarrow n\text{-}C_{18}H_{37}C_6H_5$

n-Octadecyl p-toluenesulfonate followed by $AlCl_3$ added to dry benzene, stirred 15 hrs. at room temp., 10 hrs. at 50-55°, finally 14 hrs. again at room temp. → n-octadecylbenzene. Y: 73%. D. A. Shirley and J. R. Zietz, Jr., Am. Soc. *75*, 6333 (1953).

1,1-Diaryl derivatives from oxo compounds $CO + 2\,HAr \rightarrow C(Ar)_2$

s. *2*, 664; *5*, 548; s. a. E. F. Rogers et al., Am. Soc. *75*, 2991 (1953)

Ammonium acetate *CH_3COONH_4*

Alkylidenecyanoacetic acid esters $C{:}C(CN)COOR$

s. *6*, 770; s. a. C. S. Rondestvedt, Jr., and A. H. Filbey, J. Org. Chem. *19*, 119 (1954)

Pyridine ring ○

840.

A mixture of benzaldehyde, acetophenone, NH_4-acetate, and glacial acetic acid refluxed 1 hr. → 2,4,6-triphenylpyridine. Y: 68%.—In the more sluggish reactions, acetic acid is replaced by acetamide. F. e. s. M. Weiss, Am. Soc. *74*, 200 (1952).

Acetic anhydride $(CH_3CO)_2O$

Synthesis of ethylene derivatives from aldehydes $CHO + H_2C \rightarrow CH{:}C$

s. *9*, 848

α-Nitro-β-acylaminocarboxylic acid esters from nitroacetic acid ester and aldehydes or 1,1-di(acylamino) compounds ←

841. $C_6H_5CHO + CH_3COONH_4 + CH_2(NO_2)COOC_2H_5 \xrightarrow{(CH_3CO)_2O} C_6H_5CH(NHCOCH_3)CH(NO_2)COOC_2H_5 \xleftarrow{(CH_3CO)_2O} C_6H_5CH(NHCOCH_3)_2 + CH_2(NO_2)COOC_2H_5$

NH$_4$-acetate added to a mixture of acetic anhydride, ethyl nitroacetate, and benzaldehyde,	Ethyl nitroacetate and benzylidene-bisacetamide added to acetic anhydride,

then heated 7 hrs. on a water bath → ethyl α-nitro-β-acetylamino-β-phenylpropionate (startg. m. f. 151).

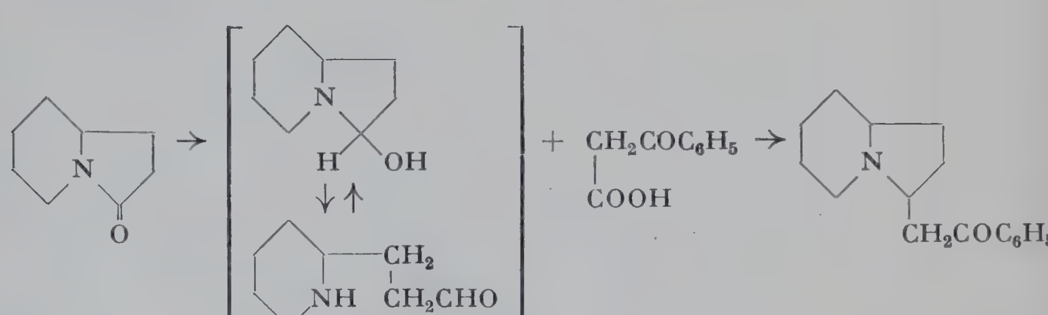
Y: 63%.	Y: 85%.

G. Stefanović and J. Bojanović, J. Org. Chem. *17*, 816 (1952); f. reactions with nitroacetic acid ester s. A. Dornow and A. Frese, A. *578*. 122 (1952).

Citrate/hydrochloric acid buffer ←

Synthesis of aminoketones via partially reduced lactams ←

842.

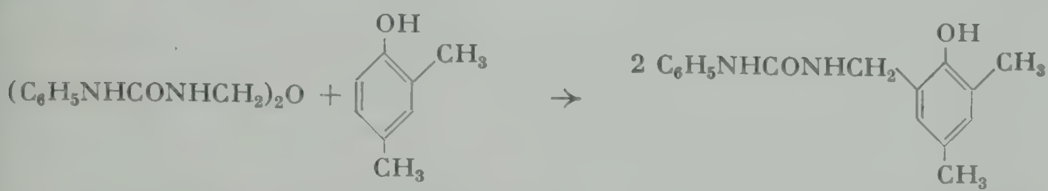


2-Oxoindolizidine allowed to react with ¼ mole + ca. 20% excess LiAlH$_4$ in abs. ether, treated with a soln. of neutralized benzoylacetic acid in citrate/HCl buffer of pH 4, the ether removed in vacuo. the aq.

soln. allowed to stand 40 hrs. at 20°, acidified to congo red reaction, and heated 20 min. on a steam bath to eliminate CO_2 → ω-(2-indolizidyl)acetophenone. Crude Y: 64%. F. e. s. F. Galinovsky, R. Weiser et al., M. *83*, 114 (1952); *82*, 551 (1951).

Formic acid *HCOOH*

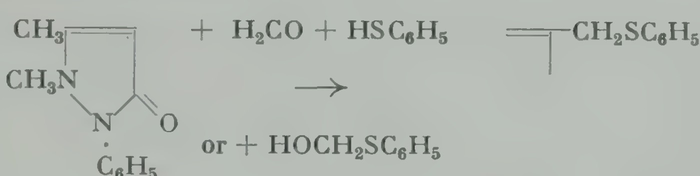
Cleavage of formaldehyde derivatives with 2,4-dimethylphenol ←

43.


Bis(phenylcarbamidomethyl) ether and 2,4-dimethylphenol in formic acid kept 2 hrs. at 50° → N-(2-hydroxy-3,5-dimethylbenzyl)-N'-phenylurea. Crude Y: 90%. F. e. s. G. Zigeuner et al., M. *82*, 847 (1951).

Acetic acid *CH_3COOH*

Thiomethylation with formaldehyde and mercaptans or hydroxymethyl thioethers H → CH_2SR

44.


A mixture of antipyrine,

phenyl mercaptan, paraformaldehyde, acetic acid, and water heated 23 hrs. on a steam bath	phenylthiomethanol, acetic acid, and water heated 23 hrs. at 100°
↘	↙

Y: 80%. 4-phenylthiomethylantipyrine. Y: 78%.

F. e. and methods, thiomethylation of phenols in the presence of triethylamine, s. F. Poppelsdorf and S. J. Holt, Soc. *1954*, 1124.

Phosphate buffer ←

Endimine ring system ○

s. 8, 816; s. a. K. Zeile and A. Heusner, B. *87*, 439 (1954)

Phosphoric acid *H_3PO_4*

Ketones from carboxylic acid anhydrides CO·O·OC → COR

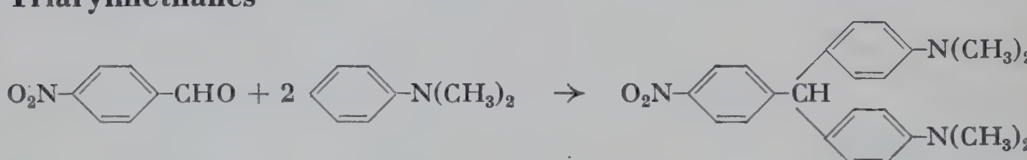
845.

Guaiacol added to a mixture of acetic anhydride and concd. H_3PO_4 (d. 1.75), refluxed 5 hrs. → acetylisoacetovanillone. Y: 28%; 67% based on startg. m. consumed.—By this procedure, the acetyl group is directed into the position para to the methoxyl group, also in the presence of a free phenolic hydroxyl group. R. Schwarz and K. Capek, M. *83*, 883 (1952).

p-Toluenesulfonic acid *TsOH*

Reactions with azeotropic water separation ←
Baeyer condensation
Triarylmethanes

846.



The Baeyer condensation proceeds smoothly in 80-90% yield when a benzene soln. of an activated ar. compound, an ar. aldehyde, and p-toluenesulfonic acid is refluxed in an apparatus equipped with a Dean-Stark water trap. The amount of water collected indicates the progress of the reaction.—E: p-Nitrobenzaldehyde and dimethylaniline → p-nitro-p′,p″-tetramethyldiaminotriphenylmethane. Y: 89%. F. e. s. E. F. Pratt and L. Q. Green, Am. Soc. *75*, 275 (1953).

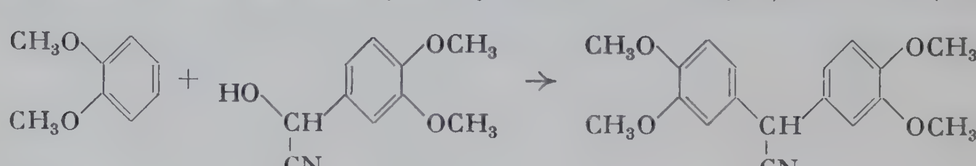
Sulfuric acid *H_2SO_4*

Alkylation of isocyclics with alcohols RH + HOR′ → R·R′

s. *2*, 678; diphenylcarbinylation s. D. G. Kundiger and E. B. W. Ovist, Am. Soc. *76*, 2501 (1954)

Synthesis of nitriles from cyanohydrins CH(CN)OH → CH(CN)R

847.

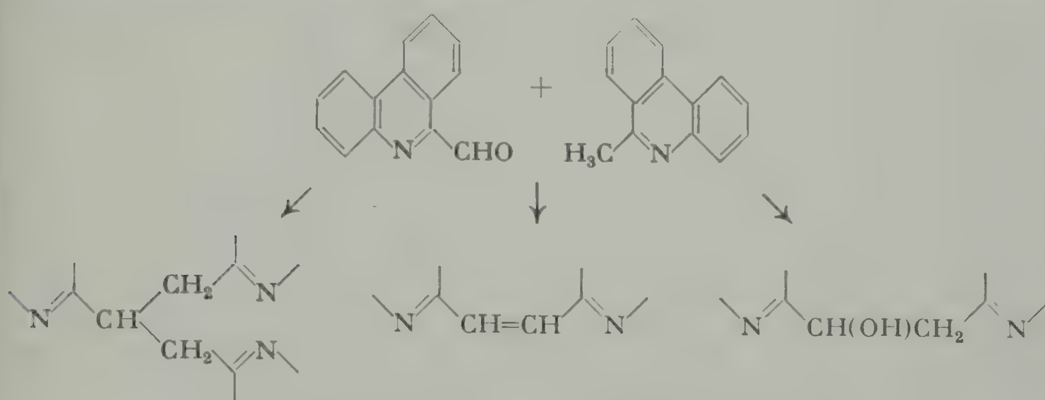


A suspension of 12 g. 3,4-dimethoxymandelonitrile in 15 ml. veratrole mixed with 74%-H_2SO_4, warmed very gradually to 70° in a water bath

with occasional stirring, and kept 30-40 min. at this temp. after complete dissolution → 18 g. bis-(3,4-dimethoxyphenyl)acetonitrile. A. Müller and M. Vajda, J. Org. Chem. *17*, 800 (1952).

Synthesis of hydrocarbons, ethylene derivatives, and sec. alcohols from aldehydes ←

8.



6-Methylphenanthridine and 6-phenanthridinealdehyde

(2 g. and 1 g.) heated 1.5 hrs. at a bath temp. of 145° with concd. H_2SO_4 → 2.1 g. 1,2,3-tri-(6-phenanthridinyl)propane.

(500 mg. each) refluxed 10 min. in acetic anhydride → 800 mg. 1,2-di-(6-phenanthridinyl)-ethylene.

(1.5 g. each) refluxed 3.5 hrs. in 80%-alcohol → 1.95 g. 1,2-di-(6-phenanthridinyl)ethanol,

F. e. s. A. G. Caldwell, Soc. *1952*, 2035.

Iodine *I*

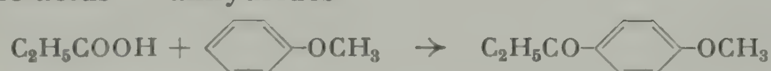
C-Acylation H → COR

of heterocyclics s. *3*, 651; of alkyl aryl ethers s. X. A. Dominguez et al., Am. Soc. *76*, 5150 (1954)

Perchloric acid $HClO_4$

Ketones from carboxylic acids — anhydrides COR

9.

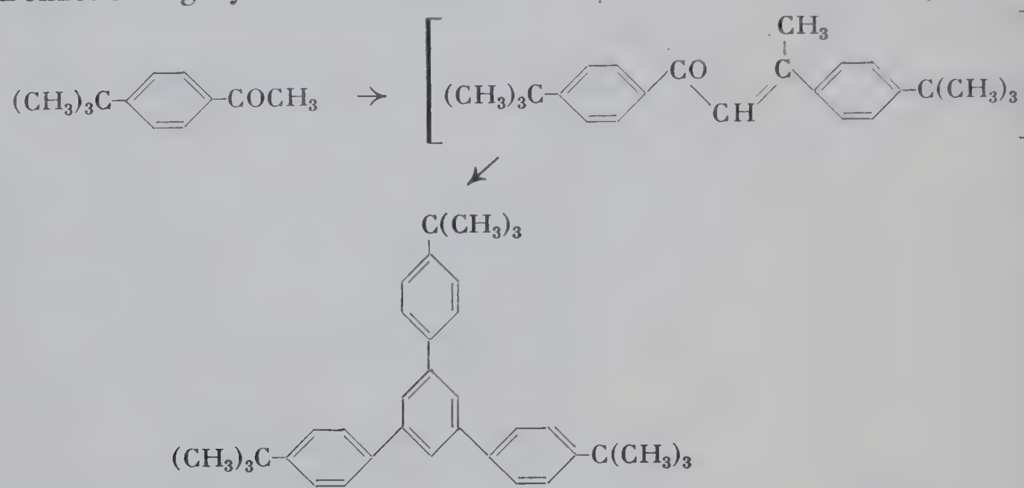


0.05 mole anisole mixed at 0° with 0.025 mole $HClO_4$, 0.2 mole propionic acid, and 0.3 mole propionic anhydride, then allowed to stand 2 hrs. at the same temp. → p-methoxypropiophenone. Y: 71%.—Somewhat lower yields, compared with other methods, are offset by the ease of operation. The reaction does not take place with acylated phenols, ar. hydrocarbons, nitrobenzene, or pyridine, nor with guaiacol. F. e. s. H. Kuhn and R. Daxner, M. *83*, 689 (1952).

Hydrochloric acid *HCl*

Benzene ring by trimerization

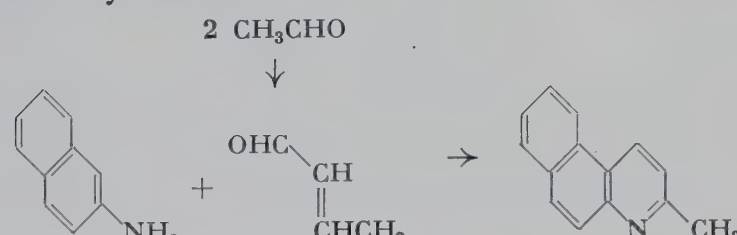
850.



p-tert-Butylacetophenone added to abs. ethanol satd. with HCl, and allowed to stand 30 days → 1,3,5-(p-tert-butylphenyl)benzene. Y: 74%. F. e. s. R. E. Lyle et al., Am. Soc. *75*, 5959 (1953).

Quinaldines
Döbner-Miller synthesis

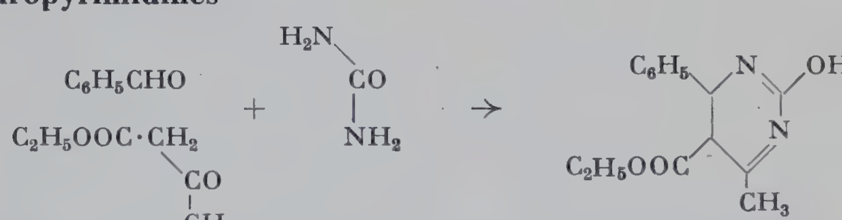
851.



β-Naphthylamine added with stirring to crude concd. HCl, heated on a steam bath, paraldehyde added dropwise with vigorous stirring, whereby the steam bath is removed temporarily to moderate the reaction, stirring continued for 7 hrs. → 5,6-benzoquinaldine. Y: 70%. M. Häring, B. Prijs, and H. Erlenmeyer, Helv. *37*, 1339 (1954).

Dihydropyrimidines

852.

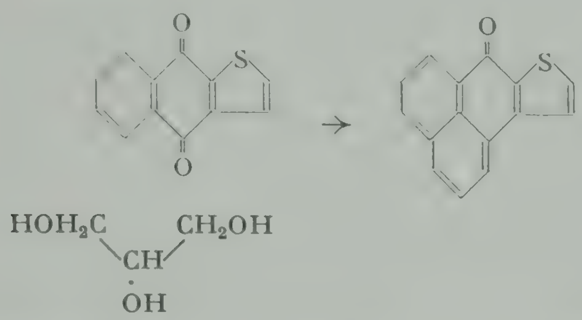


A mixture of urea, benzaldehyde, ethyl acetoacetate, ethanol, and 16 drops HCl refluxed 3 hrs. → ethyl 2-hydroxy-4-methyl-6-phenyldihydro-5-pyrimidinecarboxylate. Y: 84.5%. F. e. s. N. V. Khromov-Borisov and A. M. Savchenko, Ж. *22*, 1680 (1952); C. A. *47*, 9333d.

Iron/cupric sulfate/sulfuric acid *$Fe/CuSO_4/H_2SO_4$*

Isocyclics from quinones

53.



Glycerol and Fe-filings added uniformly over a period of 3 hrs. at 110-117° to a soln. of thiophanthraquinone in 82.5%-H_2SO_4 containing $CuSO_4$, and the reaction temp. maintained 1 hr. longer → 4,5-benzthiophanthrone. Y: 63.5%. V. Weinmayr, F. S. Palmer, and A. A. Ebert, Jr., Am. Soc. *74*, 4361 (1952).

Via intermediates *v.i.*

Gränacher synthesis via rhodanine CHO → CH_2CN

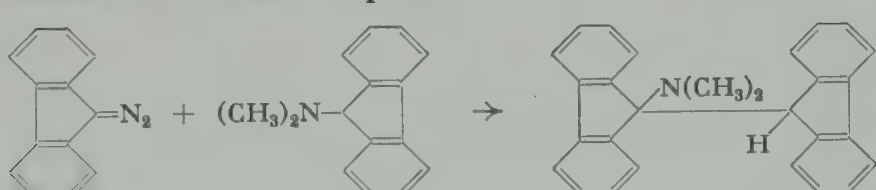
s. *3*, 662; s. a. M. F. Grundon and H. J. H. Perry, Soc. *1954*, 3531

Nitrogen ↑ CC⇅N

Without additional reagents *w.a.r.*

Tert. amines from diazo compounds ←

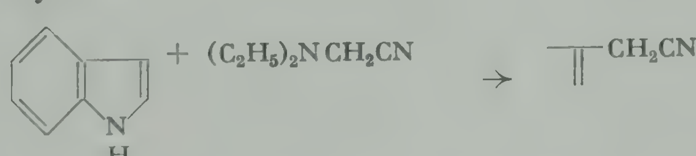
54.



9-Diazofluorene added portionwise to 9-fluorenyldimethylamine at ca. 150° so that a steady reaction is maintained without further external heating → 9-dimethylamino-9,9′-bifluorene. Y: 45%. F. e. s. W. R. Bamford and T. S. Stevens, Soc. *1952*, 4675.

C-Cyanomethylation H → CH_2CN

55.

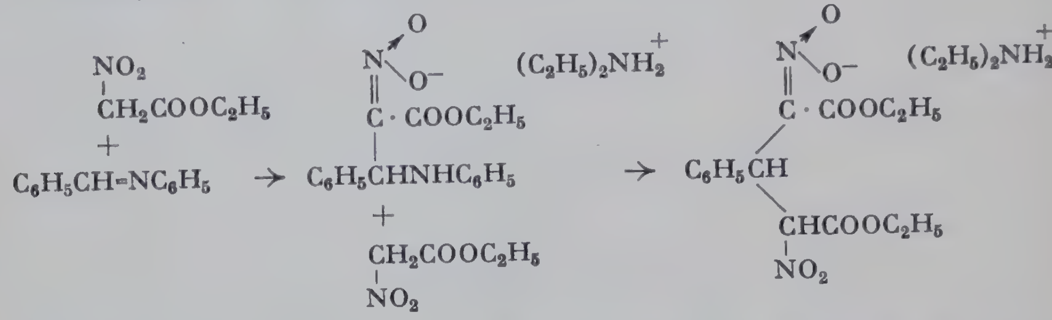


A mixture of indole and diethylaminoacetonitrile heated 6 hrs. at ca. 170° under N_2 → indole-3-acetonitrile. Y: 33-44%. E. L. Eliel and N. J. Murphy, Am. Soc. *75*, 3589 (1953).

←

Reactions of nitroacetic acid ester
Salts of aci-α-γ-dinitroglutaric acid esters
from nitroacetic acid ester and azomethines
or aldehydes

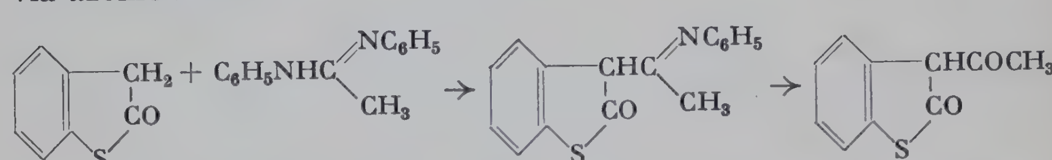
856.



Benzylideneaniline allowed to react for a few hrs. with 2 moles nitroacetic acid ester and diethylamine in a mixture of abs. alcohol and ether → diethylammonium salt of *aci-α,γ*-dinitro-*β*-phenylglutaric acid ester. Y: 94-98%. F. e., also isolation of the intermediates, s. A. Dornow and A. Frese, A. *578*, 122 (1952); from aldehydes s. A. *578*, 113; f. reactions s. a. A. *578*, 101.

Synthesis of oxo compounds CH → C·COR
from hydrocarbons and amidines
via azomethines

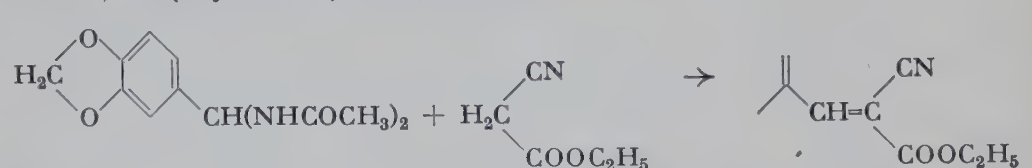
857.



A mixture of thioöxindole (prepn. s. 121) and N,N′-diphenyl-formamidine in ethanol refluxed 15 min. → thioöxindole-3-aldehyde anil (Y: 70-78%) refluxed 1 hr. in aq.-alc. KOH → thioöxindole-3-aldehyde (Y: 72%). With N,N′-diphenylacetamidine at 140-150° without solvent → anil (Y: 64%) hydrolyzed as above → 3-acetylthioöxindole (Y: 88-96%). F. e. s. R. H. Glauert and F. G. Mann, Soc. *1952*, 2127.

***α,β*-Ethylene-*α*-cyanocarboxylic acid esters** $C(NHAc)_2 \rightarrow C{:}C(CN)COOR$
from 1,1-di(acylamino) compounds

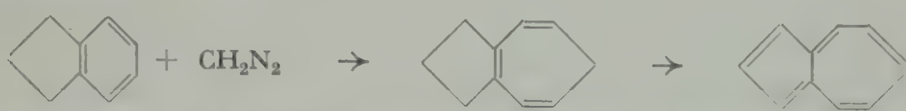
858.



3,4-Methylenedioxybenzylidenebisacetamide and ethyl cyanoacetate heated 8 hrs. in an oil bath at 140-150° → ethyl *α*-cyano-*β*-(3,4-methylenedioxyphenyl)acrylate. Crude Y: 90.8%. F. e., with lower yields, s. G. Stefanović and Z. Nikić, J. Org. Chem. *17*, 1305 (1952).

Irradiation ←

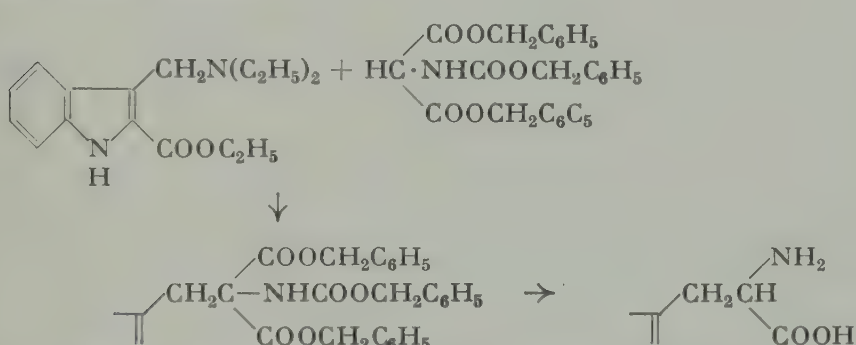
Two-step azulene synthesis ←
Ring expansion of isocyclics
Dehydration

859. 

Nitrosomethylurea added in several portions over a period of 1 hr. to a mixture of indane and aq. 50%-KOH, stirred another hr., the organic layer separated and irradiated 24 hrs. with sun lamps → trimethylenetropilidene dropped on a column of 5%-Pd on coconut charcoal at 340°/20 mm. during 1 hr. → azulene. Y: 6.7% based on indane consumed. W. von E. Doering, J. R. Mayer, and C. H. DePuy, Am. Soc. 75, 2386 (1953).

Sodium hydride *NaH*

Synthesis of α-aminocarboxylic acids with tert. amines $CH_2N(R)_2 \rightarrow CH_2CH(NH_2)COOH$
Simultaneous cleavage of carbobenzoxy derivatives of amines and benzyl esters

860. 

A soln. of dibenzyl carbobenzoxyaminomalonate and 2-carbethoxy-3-diethylaminomethylindole in dry xylene containing a trace of NaH refluxed, while a stream of N_2 is bubbling through, until after 3.5 hrs. the theoretical amount of diethylamine has been given off → condensation product (Y: 89%) hydrogenated with 10%-Pd-on-charcoal in dry methanol for 3 hrs., and a soln. of the crude product in benzene evaporated three times to dryness → 2-carbethoxytryptophan (Y: 76%). F. e. s. H. M. Kissman and B. Witkop, Am. Soc. 75, 1967 (1953).

Sodium hydroxide *NaOH*

Syntheses with tert. amines ←

s. 6, 789; s. a. H. Hellmann and E. Brendle, H. 287, 235 (1951); with diethyl formamidomalonate s. a. A. Ek and B. Witkop, Am. Soc. 76, 5579 (1954)

H → CH_2CH_2COR

C-β-Acylethylation
γ-Nitroketones from tert. amines

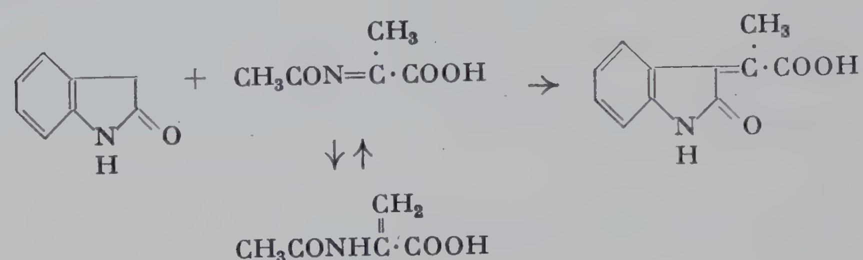
861. $$C_6H_5COCH_2CH_2N(CH_3)_2 + \underset{NO_2}{\underset{|}{HC}}(CH_3)_2 \rightarrow C_6H_5COCH_2CH_2\underset{NO_2}{C}(CH_3)_2$$

A soln. of β-dimethylaminopropiophenone in excess 2-nitropropane containing solid NaOH refluxed 6.5 hrs. in an N_2-atmosphere until evolution of volatile base ceases → 2-methyl-2-nitro-5-phenyl-5-pentanone. Y: 82%. F. e. s. N. S. Gill et al., Am. Soc. *74*, 4923 (1952).

Sodium/alcohol *NaOR*

Isatylidene compounds ←

862.

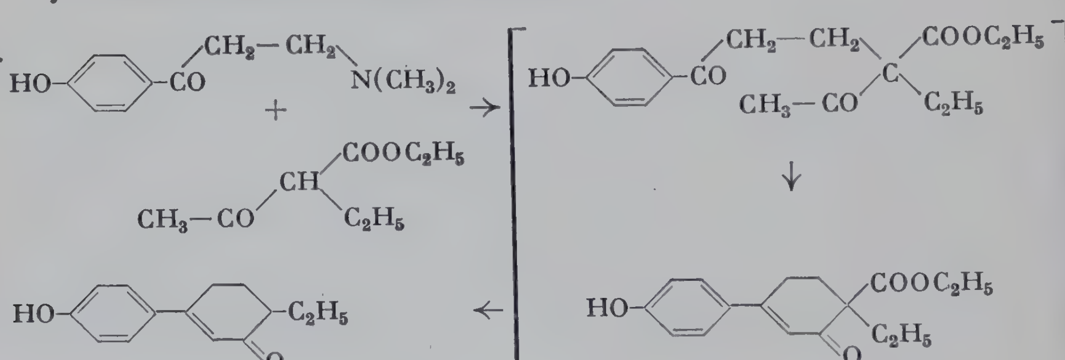


Oxindole dissolved in a soln. of Na in abs. alcohol, α-acetamidoacrylic acid added, and refluxed 6 hrs. under N_2 → Na-isatylidenemethylacetate. Y: 97%. F. e. s. P. L. Julian et al., Am. Soc. *75*, 5305 (1953).

Potassium tert-butoxide *KOR*

Cyclohexenones from β-aminoketones ○

863.



A mixture of β-dimethylamino-p-hydroxypropiophenone hydrochloride, ethyl α-ethylacetoacetate, and K-*tert*-butoxide in dioxane refluxed 24 hrs. → 3-(p-hydroxyphenyl)-6-ethyl-2-cyclohexen-1-one. Y: 71.4%.—If the product does not crystallize, it is saponified with aq. alkali for 2 hrs. to eliminate the carbalkoxy group completely. F. e. s. F. C. Novello, M. E. Christy, and J. M. Sprague, Am. Soc. *75*, 1330, 5431 (1953).

Phenyllithium *C_6H_5Li*

Introduction of aldehyde groups into ar. nuclei H → CHO

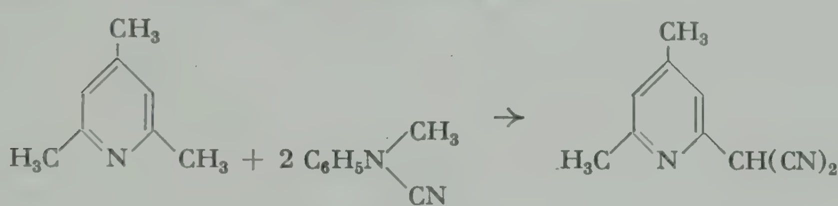
864.

A soln. of 5-methoxy-2-thienyl-Li prepared from 2-methoxythiophene and phenyl-Li (from Li and bromobenzene) in ether added in a slow stream with efficient stirring to an ice-cold soln. of a slight excess of dimethylformamide in ether, and left at room temp. overnight → 5-methoxy-2-thenaldehyde. Y: 67%.—The secondary products (dimethylamine and unreacted dimethylformamide) are water soluble, which simplifies the isolation of the aldehyde. J. Sicé, Am. Soc. *75*, 3697 (1953).

s. *2*, 694; s. a. J. P. Lambooy, Am. Soc. *76*, 133 (1954)

Nitriles from organometallic compounds ←
Replacement of hydrogen by cyano groups

865.

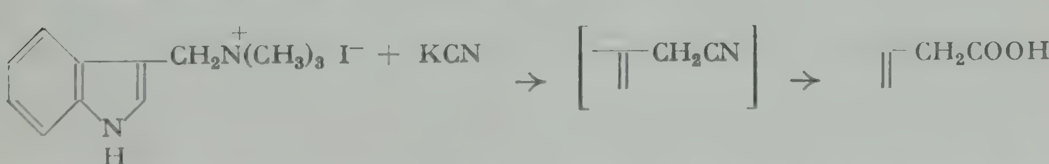


Collidine treated under N_2 at room temp. with an ethereal *N* phenyl-Li soln., allowed to stand 1 hr. at room temp., then treated at –15° with an ethereal soln. of N-methyl-N-cyanoaniline, and the product isolated after 24 hrs. → (4,6-dimethyl-2-pyridyl)malondinitrile. Y: 70%.—Compared with cyanogen chloride, N-methyl-N-cyanoaniline has the advantage of easier handling and dosage. F. e., also mononitriles, s. H. Lettré, P. Jungmann, and J.-C. Salfeld, B. *85*, 397 (1952).

Alkali cyanide ←

Carboxylic acids from quaternary ammonium salts via nitriles $\overset{+}{N}R_3$ → COOH
Synthesis with addition of 1 C-atom

866.



Gramine methiodide added to a soln. of KCN in 60% aq. ethanol, then a N_2-stream passed through for 24 hrs. whereby trimethylamine is removed, aq. 20%-KOH added, and refluxed 10 hrs. → 3-indoleacetic acid.

Y: 76%. T. A. Geissman and A. Armen, Am. Soc. *74*, 3916 (1952); without KOH in an autoclave at 150-160° s. A. P. Terent'ev, A. N. Kost, and S. M. Gurvich, Ж. *23*, 615 (1953); with NaCN s. J. Thesing and F. Schülde, B. *85*, 324 (1952); phthalimidoacetonitriles s. H. Hellmann, J. Löschmann, and F. Lingens, B. *87*, 1691 (1954).

Copper *Cu*

α,β-Ethylene-γ-diketones from α-diazoketones Dimerization $2 \cdot COCHN_2 \rightarrow \cdot COCH{:}CHCO\cdot$

867. $2\ C_6H_5COCHN_2 \rightarrow C_6H_5COCH{=}CHCOC_6H_5$

α-Diazoacetophenone in benzene treated with Cu-bronze (Naturkupfer C) at 65-70° → *trans*-1,2-dibenzoylethylene. Y: 70%. P. Yates, Am. Soc. *74*, 5376 (1952).

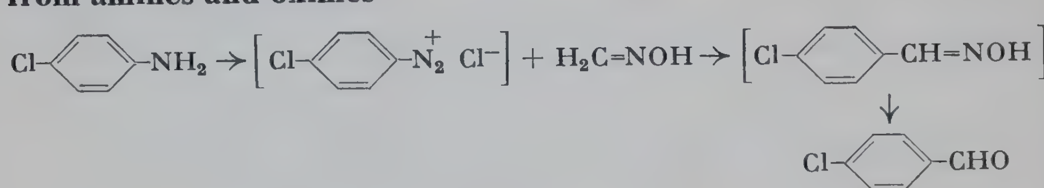
Cuprous cyanide *CuCN*

Replacement of amino by cyano groups $NH_2 \rightarrow CN$

s. *3*, 666; s. a. R. H. Miller and O. Gisvold, J. Am. Pharm. Assoc. *42*, 367 (1953)

Cupric sulfate *CuSO₄*

Synthesis of oxo compounds from amines and oximes $NH_2 \rightarrow CO$

868. 

A soln. of p-chlorobenzenediazonium chloride, prepared from p-chloroaniline, HCl, and ice-water by treatment with aq. $NaNO_2$ at 0-5°, neutralized towards Congo-red by addition of aq. Na-acetate, introduced at 10-15° with stirring below the surface of aq. formaldoxime to which has been added Cu-sulfate, some Na-sulfite, and Na-acetate, stirring continued for 1 hr., acidified with excess HCl, then refluxed 2 hrs. → p-chlorobenzaldehyde. Y: 60%. F. e. s. W. F. Beech, Soc. *1954*, 1297.

Cupric chloride *$CuCl_2$*

Diazo coupling 1,4-Addition ←

s. *4*, 760; s. a. E. A. Braude, J. S. Fawcett, and A. A. Webb, Soc. *1954*, 1049

Acetic anhydride *$(CH_3CO)_2O$*

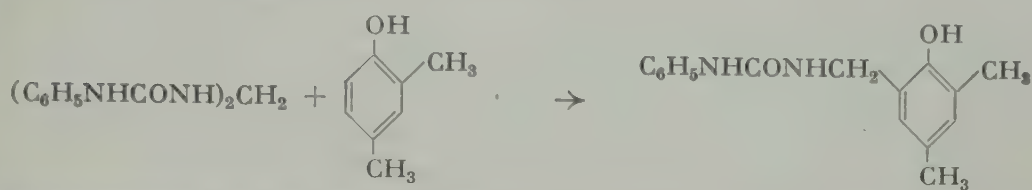
Syntheses with 1,1-di(acylamino) compounds ←

s. 9, 841; s. a. J. Org. Chem. *17*, 1114 (1952)

Formic acid *HCOOH*

Cleavage of formaldehyde derivatives with 2,4-dimethylphenol ←

869.

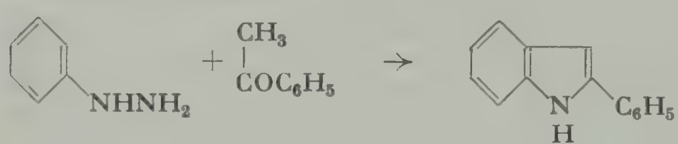


Methylenebis(phenylurea) and 2,4-dimethylphenol in formic acid kept 2 hrs. at 50° → N-(2-hydroxy-3,5-dimethylbenzyl)-N′-phenylurea. Y: 95%. F. e. s. G. Zigeuner et al., M. *82*, 494 (1951).

Polyphosphoric acid *$H(PO_3H)_xOH$*

Fischer indole ring synthesis

870.



Polyphosphoric acid added to a mixture of acetophenone and phenylhydrazine, stirred and warmed gently until a sudden rise of temp. indicates beginning of the reaction, then the temp. kept at 180° by water-cooling → 2-phenylindole. Y: 76%. F. e. s. H. M. Kissman, D. W. Farnsworth, and B. Witkop, Am. Soc. *74*, 3948 (1952); from hydrazones s. J. Org. Chem. *19*, 1824 (1954).

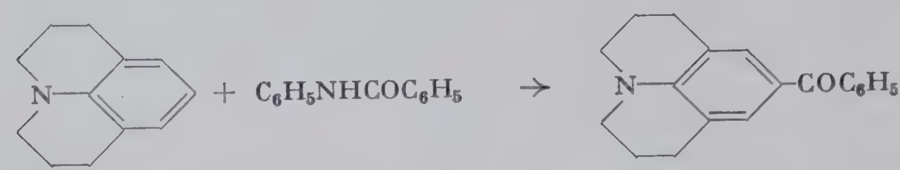
Phosphorus oxychloride *$POCl_3$*

Aldehyde synthesis with dimethylformamide H → CHO

871.

$POCl_3$ added dropwise with stirring and cooling to dimethylformamide, then technical dimethylaniline added dropwise with stirring, and heated 2 hrs. with stirring on a steam bath → p-dimethylaminobenzaldehyde. Y: 70.5%.—Dimethylformamide gives somewhat lower yields than N-methylformanilide but has the advantage of being inexpensive. F. e. s. E. Campaigne and W. L. Archer, Am. Soc. *75*, 989 (1953); s. a. Org. Synth. *33*, 27 (1953); F. T. Tyson and J. T. Shaw, Am. Soc. *74*, 2273 (1952); W. E. Parham and V. J. Traynelis, Am. Soc. *76*, 4960 (1954).

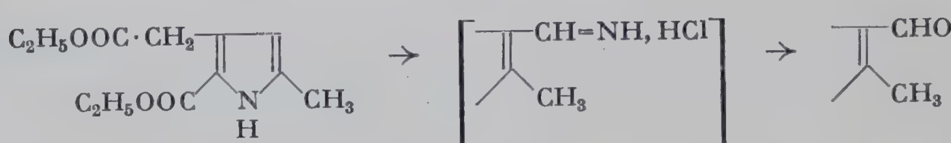
Synthesis of ketones from carboxylic acid amides H → COR

872. 

A mixture of julolidine, benzanilide, and $POCl_3$ heated 1 hr. at 120°, then boiled a short time with concd. HCl → 9-benzoyljulolidine. Y: 70%.—Friedel-Crafts synthesis was not successful. F. e. s. P. A. S. Smith and Tung-Yin Yu, J. Org. Chem. *17*, 1281 (1952).

Hydrochloric acid *HCl*

Fischer-Zerweck aldehyde synthesis H → CHO

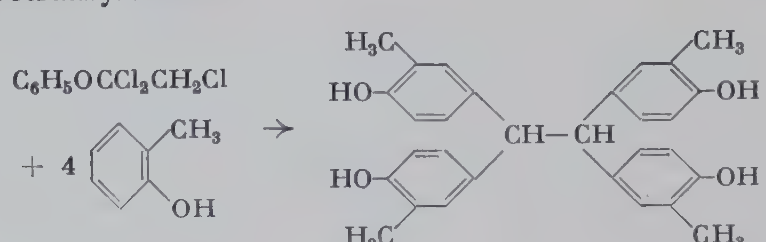
873. 

A slow current of HCl passed for 2 hrs. with ice-salt cooling and frequent shaking into a soln. of ethyl 4-carbethoxymethyl-2-methylpyrrole-5-carboxylate in dry ether-chloroform-HCN, HCl passed in at an increased rate, while crystals separate and for 2 hrs. thereafter, the aldimine hydrochloride filtered off, washed with ether, dried in vacuo, dissolved in ice-water, quickly filtered, and the pH brought to 4 → 5-carbethoxy-4-carbethoxymethyl-2-methylpyrrole-3-aldehyde. Y: 97%. S. F. MacDonald, Soc. *1952*, 4184.

Halogen ↑ CC ⇅ Hal

Without additional reagents *w.a.r.*

1,1,2,2,Tetraarylethanes $Ar_2CHCHAr_2$

874. 

2 g. α,α,β-trichloroethyl phenyl ether and 3.8 g. o-cresol allowed to react at 50° for 3 hrs. → 3 g. 1,1,2,2-tetrakis-(3-methyl-4-hydroxy-

phenyl)ethane. E. Ziegler, W. Kaufmann, and N. Kreisel, M. *83*, 1274 (1952).

Synthesis of α,β-ethyleneketones from carboxylic acid chlorides COCl → COCH:C

875. $(C_6H_5)_2C{=}CH_2 + ClCOC_6H_5 \rightarrow (C_6H_5)_2C{=}CHCOC_6H_5$

A mixture of 1,1-diphenylethylene and benzoyl chloride heated 30 hrs. at 190-200° while dry N_2 is bubbled through → 1-benzoyl-2,2-diphenylethylene. Y: 46%.—The condensation could not be performed with satd. aliphatic acyl chlorides because of their thermal instability. F. e. s. F. Bergmann, S. Israelashvili, and D. Gottlieb. Soc. *1952*, 2522.

2-Acylamino-1,3-diols from carboxylic acids via α-bromocarboxylic acid bromides, α-diazo-β-keto-γ-bromocarboxylic acid esters, and α-amino-β-ketocarboxylic acid esters ←

876. $n{-}C_{14}H_{29}CH_2COOH \rightarrow n{-}C_{14}H_{29}CHBrCOBr + N_2CHCOOC_2H_5$

$$\downarrow$$

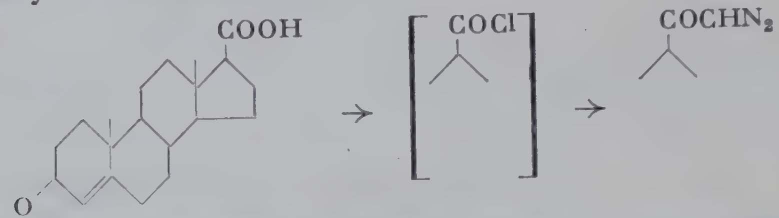
$$n{-}C_{14}H_{29}CH_2CO\underset{\substack{|\\ NH_2,\,HCl}}{C}HCOOC_2H_5 \leftarrow n{-}C_{14}H_{29}CHBrCO\underset{\substack{\|\\ N_2}}{C}\cdot COOC_2H_5$$

$$\downarrow$$

$$n{-}C_{14}H_{29}CH_2CO\underset{NHCOCH_3}{C}HCOOC_2H_5 \rightarrow n{-}C_{14}H_{29}CH_2CH(OH)\underset{NHCOCH_3}{C}HCH_2OH$$

Palmitic acid allowed to react with dry red P and Br → crude α-bromopalmitoyl bromide (Y: 96.5%) added at 15-18° with vigorous stirring during 3.5-4 hrs. to crude ethyl diazoacetate, stirring continued 3 hrs. at 20°, allowed to stand overnight at the same temp., then warmed at 30-35° with stirring until N_2-evolution ceases → crude ethyl DL-2-diazo-3-oxo-4-bromostearate (Y: 72.8%) hydrogenated with prehydrogenated Pd-on-carbon in alcohol containing HCl → crude ethyl DL-2-amino-3-oxostearate hydrochloride shaken 5 hrs. with acetic anhydride and Ag-acetate in methanol at room temp. in the dark → ethyl DL-2-acetamino-3-oxostearate dissolved in abs. tetrahydrofuran, added dropwise with vigorous stirring at 20-30° during 15 min. to a soln. containing $NaBH_4$ and LiI in tetrahydrofuran, stirring continued 5 hrs. at 20°, then allowed to stand overnight → mixture of racemates of 2-acetaminooctadecane-1,3-diols (Y: 89%). Over-all Y: 26%. I. Sallay, F. Dutka, and G. Fodor, Helv. *37*, 778 (1954); reduction with $NaBH_4$/LiI s. a. J. Kollontitsch, O. Fuchs, and V. Gábor, Nature *173*, 125 (1954).

α-Diazoketones from carboxylic acids via carboxylic acid chlorides COOH → $COCHN_2$

877. 

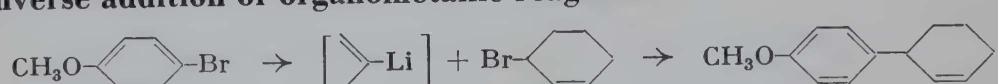
Abs. benzene poured over 3-keto-4-etienic acid, then oxalyl chloride added at 0° under anhydrous conditions, kept 20 min. at 20° with occasional swirling until dissolved, then an additional 20 min. at the same temp., evaporated in vacuo, dissolved in benzene, added at –10° to ethereal diazomethane (prepn. s. original), and allowed to stand 1 hr. at 20° ⟶ 21-diazoprogesterone. Y: 75%.—Neither use of the Na-salt of the acid, nor addition of pyridine (cf. Synth. Meth. *7*, 583) was advantageous for the preparation of the acid chloride. F. e. s. F. Reber, A. Lardon, and T. Reichstein, Helv. *37*, 45 (1954).

Arndt-Eistert synthesis COOH → CH_2COOR

s. *2*, 771; *1*, 190; with α-aminoacids s. K. Balenović and D. Dvornik. Soc. *1954*, 2976

Lithium *Li*

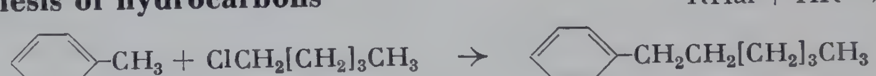
Synthesis of hydrocarbons from halides RHal + HalR′ → R·R′
Inverse addition of organometallic reagents

878. 

p-Methoxyphenyl-Li, prepared from p-methoxyphenyl bromide and Li in ether under N_2, added dropwise to a vigorously stirred ethereal soln. of 3-bromocyclohexene, and refluxing continued for 2 hrs. → 3-(p-methoxyphenyl)cyclohexene. Y: 71%.—Inverse addition of the organometallic compound gives better yields, an effect particularly marked with Grignard reagents. F. e. s. W. R. Biggerstaff, A. P. Menditto, and I. Yokoyama, J. Org. Chem. *19*, 934 (1954).

Sodium/potassium isopropoxide *Na/KOR*

Synthesis of hydrocarbons RHal + HR′ → R·R′

879. 

K-isopropoxide added to Na-sand in sulfur-free toluene, then n-amyl chloride added dropwise with vigorous stirring and cooling at 20°, and stirring continued for 45 min. ⟶ n-hexylbenzene. Y: 76%. F. additional reagents s. A. A. Morton and A. E. Brachman, Am. Soc. *73*, 4363 (1951); *76*, 2980 (1954).

Sodium hydride *NaH*

Synthesis of hydrocarbons via 1,1-disulfones ←

880. $$(CH_3)_2CHCH_2CH_2Br + H_2C(SO_2C_2H_5)_2 \rightarrow (CH_3)_2CHCH_2CH_2CH(SO_2C_2H_5)_2 + (CH_3)_2CHCH_2CH_2Br$$
$$\downarrow$$
$$(CH_3)_2CH[CH_2]_5CH(CH_3)_2 \leftarrow [(CH_3)_2CHCH_2CH_2]_2C(SO_2C_2H_5)_2$$

Molar equivalents of Na-bis(ethylsulfonyl)methane and isoamyl bromide thoroughly mixed in dimethylformamide, and stirring continued at 80-90° for 1 hr. → 1,1-bis(ethylsulfonyl)-4-methylpentane (startg. m. f. 767) (Y: 85%) added to an ice-cooled suspension of NaH in dimethylformamide, the ice bath removed after 5 min., stirred 2-3 hrs., isoamyl bromide added, and stirring continued at 90-95° for 18 hrs. → 5,5-bis(ethylsulfonyl)-2,8-dimethylnonane (Y: 72%) heated 36 hrs. with Raney-Ni in cyclohexane at 250° and 2500 p. s. i. H_2 → 2,8-dimethylnonane (Y: 78%). F. e., also without isolation of the monoalkylated bis(ethylsulfonyl)methane, and partial desulfuration, s. M. W. Cronyn, Am. Soc. *74*, 1225 (1952); J. Org. Chem. *19*, 139 (1954); hydrogenation cf. Synth. Meth. *9*, 378.

Synthesis of ketones from carboxylic acid chlorides with t-butyl malonates Alkylation of malonic acid esters Blocking of carboxyl groups ←

881. $$C_6H_5CH_2Cl + H_2C[COOC(CH_3)_3]_2 \rightarrow C_6H_5CH_2CH[COOC(CH_3)_3]_2 + ClCOC_6H_5$$
$$\downarrow$$
$$(C_6H_5CH_2)(C_6H_5CO)CH_2 + 2\ CO_2 + 2\ CH_2{=}C(CH_3)_2 \leftarrow (C_6H_5CH_2)(C_6H_5CO)C[COOC(CH_3)_3]_2$$

A soln. of benzyl chloride in dry t-butyl alcohol added to a soln. of di-t-butyl sodiomalonate prepared from di-t-butyl malonate and NaH in t-butyl alcohol, and stirred 1.5 hrs. at ca. 65° → di-t-butyl benzylmalonate (Y: 80%) dissolved in dry benzene, treated with NaH, gently stirred and heated ca. 2.5 hrs. at ca. 80° until gas evolution ceases, a soln. of benzoyl chloride in benzene added, heating and stirring continued for 1 hr., cooled to room temp., excess NaH destroyed by the addition of anhydrous p-toluenesulfonic acid, filtered, washed with benzene, benzene evaporated, and the residue refluxed 1 hr. with an-

hydrous p-toluenesulfonic acid in glacial acetic acid containing ca. 2% acetic anhydride → phenyl β-phenylethyl ketone (Y: 80%). F. e. s. G. S. Fonken and W. S. Johnson, Am. Soc. 74, 831 (1952).

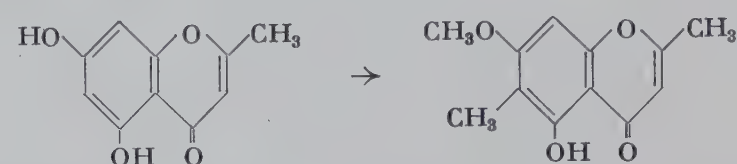
Synthesis of α-aminocarboxylic acids ←

s. 8, 841; s. a. Am. Soc. 76, 3484 (1954)

Potassium hydroxide *KOH*
s. Potassium iodide/potassium hydroxide
and copper/potassium hydroxide

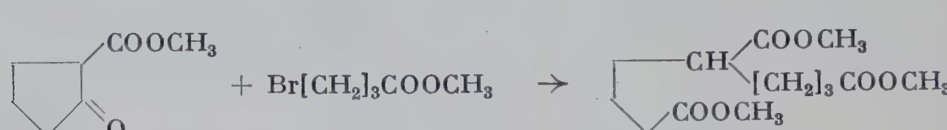
Sodium/alcohol *NaOR*

Simultaneous C- and O-methylation ←

882. 

A soln. of 0.5 g. 5,7-dihydroxy-2-methylchromone in methanol and methyl iodide containing Na refluxed 12 hrs. → 0.4 g. 5-hydroxy-7-methoxy-2,6-dimethylchromone. W. B. Whalley, Am. Soc. 74, 5795 (1952).

Synthesis of dicarboxylic acid esters
from cyclic β-ketocarboxylic acid esters
Hydrolytic ring opening of isocyclics C

883. 

47.5 g. methyl 2-ketocyclopentanecarboxylate added rapidly to a soln. of Na in anhydrous methanol, stirred for a few min., 60.5 g. methyl 4-bromobutyrate added, refluxed 3 hrs., and allowed to stand overnight → 56 g. trimethyl δ-carboxyazelate (Y: 70%) and 19 g. methyl adipate. J. F. Tinker, Am. Soc. 73, 4493 (1951).

Sodium compound ←

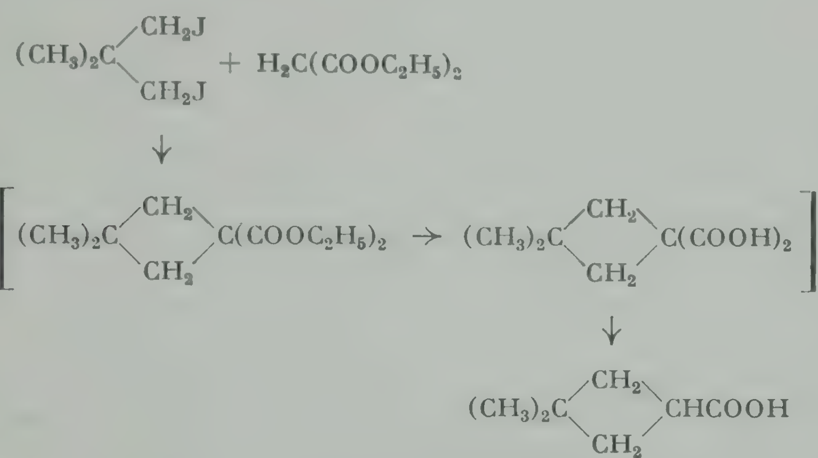
Synthesis of hydrocarbons ←
via 1,1-disulfones

s. 9, 880

Potassium isobutoxide *KOR*

Cycloalkanecarboxylic acids by malonic acid synthesis

84.



Ethyl malonate followed by 1,3-diiodo-2,2-dimethylpropane (prepn. s. Synth. Meth. *8*, 616) added to a soln. of K in anhydrous isobutanol, refluxed with stirring for 100 hrs., aq.-alc. (1:1) KOH added, refluxing continued for 8 hrs., and the isolated crude 3,3-dimethylcyclobutane-1,1-dicarboxylic acid decarboxylated at 180° for 1 hr. → 3,3-dimethylcyclobutanecarboxylic acid. Y: 73%; average for 4 runs, 61%.—Substitution of tert-butanol for isobutanol reduced the yield to 11%. A. Campbell and H. N. Rydon, Soc. *1953*, 3002; cf. V. P. Gol'mov, Ж. *23*, 1162 (1953); C. A. *47*, 12255e; H. Pommer, A. *579*, 47 (1953); with dibromides cf. S. F. Birch, R. A. Dean, and E. V. Whitehead, J. Org. Chem. *19*, 1449 (1954).

Potassium tert-butoxide

Alkylation of β-ketocarboxylic acid esters ·HC(COR)COOR → ·RC(COR)COOR

s. *3*, 677/8; s. a. H. Plieninger and C. E. Castro, B. *87*, 1760 (1954)

Potassium isopropoxide/sodium *KOR/Na*

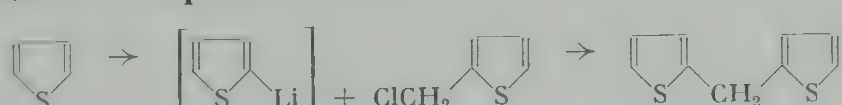
s. Sodium/potassium isopropoxide

Butyllithium C_4H_9Li

Synthesis of hydrocarbons from halides RHal + HR′ → R·R′

Metalation of thiophenes

85.



Thiophene allowed to react with n-butyl-Li in ether under N_2, then α-chloromethylthiophene added slowly to the cooled soln., and refluxed

40 hrs. until the test of organo-Li compounds is negative → 2,2′-methylenedithiophene. Y: 66%. N. Löfgren and C. Tegner, Acta Chem. Scand. *6*, 1020 (1952).

Syntheses with lithium alkenyls ←

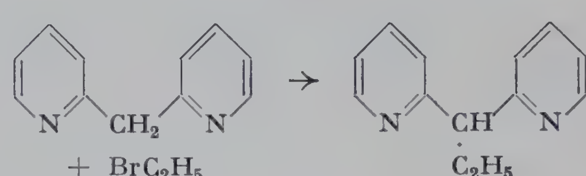
886. $C_6H_5CH{=}CHBr \rightarrow C_6H_5C{\equiv}C{\cdot}COOH$

α,β-Acetylenecarboxylic acids from α,β-ethylenehalides. A soln. of butyl-Li in ether added at −35° over a period of 4.5 min. to a mixture of *cis*- and *trans*-ω-bromostyrene dissolved in ether, after an additional 1.5 min. poured onto Dry Ice, and the product isolated as the anilinium salt → anilinium phenylpropiolate. Y: 45%. F. syntheses without dehydrohalogenation s. D. Y. Curtin and E. E. Harris, Am. Soc. *73*, 4519 (1951). *trans* and *cis* ethylene derivatives with Li cf. A. S. Dreiding and R. J. Pratt, Am. Soc. *76*, 1902 (1954).

Phenyllithium C_6H_5Li

Synthesis of hydrocarbons from halides RHal + HR′ → ·RR′
Metalation

887.



6.0 g. 2,2′-dipyridylmethane added slowly at 0° to ethereal phenyl-Li (from bromobenzene and Li), after stirring for 30 min. ethyl bromide in ether added, and stirred 6 hrs. at room temp. → 5.9 g. 1,1-di-2-pyridylpropane. F. e. s. E. Leete and L. Marion, Can. J. Chem. *30*, 563 (1952); 4-alkylpyridines s. J. P. Wibaut and J. W. Hey, R. *72*, 513 (1953).

Alkylation of Reissert compounds H→R

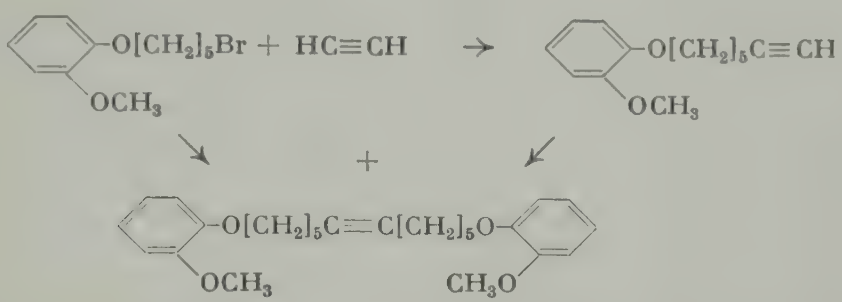
s. *9*, 581

Dimerization of halides ←
Isocyclics from halides

s. *9*, 966

Sodium amide *$NaNH_2$*

Synthesis of acetylene derivatives from halides ←



Na (> 2 moles) converted into a suspension of Na-acetylide in liq. NH_3 in the presence of a little $Fe(NO_3)_3$, then treated dropwise with stirring during 1.5 hrs. with 5-o-methoxyphenoxypentyl bromide (prepn. s. 312) in twice its bulk of dry ether, more ether added to replace the liq. NH_3 lost by evaporation, allowed to warm to room temp. overnight, finally gently refluxed 1.5 hrs. on a steam bath → 7-o-methoxyphenoxyhept-1-yne (Y: 93% based on startg. m. consumed) in twice its bulk of dry ether added during 1 hr. to $NaNH_2$ prepared from Na in liq. NH_3, with stirring, which is continued for a further hr., then 5-o-methoxyphenoxypentyl bromide in twice its volume of ether run in during 30 min., stirred overnight, and refluxed 4 hrs. → 1,12-di-o-methoxyphenoxydodec-6-yne (Y: ca. 100%).—In general, it is advantageous to use 2-2.2 times the calculated amount of $NaNH_2$, whereby the product is obtained purer and in better yield. F. e. s. A. W. Nineham, Soc. *1953*, 2601.

Alkylation

of ketones COCH → COCR

s. *1*, 655; s. a. K. E. Hamlin and M. Freifelder, Am. Soc. *75*, 369 (1953)

of nitriles CHCN → CRCN

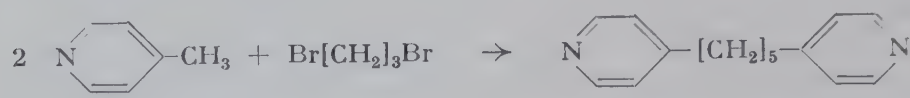
s. *1*, 656; *3*, 680; *4*, 774; s. a. N. Sperber and R. Fricano, Am. Soc. *75*, 2986 (1953); F. B. Tutwiler, R. G. Child, and S. N. Wrenn, J. Org. Chem. *19*, 910 (1954)

α-Side chain alkylation of pyridines

s. *8*, 851; s. a. H. L. Lochte and E. N. Wheeler, Am. Soc. *76*, 5548 (1954)

Potassium amide *KNH_2*

Polymethylenebipyridines ←

889. 

4-Picoline added with stirring at -80^0 to liq. NH_3 containing KNH_2, stirring continued for 10 min., trimethylene dibromide in ether slowly added, and stirred for 3 more hrs. at -80^0 ⟶ 4,4′-pentamethylenebipyridine. Y: 64%. F. e. s. L. M. Jampolsky et al., Am. Soc. *74*, 5222 (1952).

Selective alkylation of ketones via α-alkoxymethyleneketones ←

s. *4*, 775; s. a. V. Sýkora et al., Collection Czechoslov. Chem. Communs. *19*, 566 (1954)

Potassium carbonate *K_2CO_3*

Alkylation of α-cyanocarboxylic acid esters ·HC(CN)COOR → ·R′C(CN)COOR

s. *6*, 802; s. a. P. E. Gagnon, G. Nadeau, and R. Côté, Can. J. Chem. *30*, 592 (1952)

Sodium cyanide *NaCN*

Replacement of halogen by cyano groups Hal → CN

890. n-Butyl bromide stirred and refluxed 1 hr. with NaCN in *ethylene glycol* ⟶ valeronitrile. Y: 90%. F. e., also from sec. and tert. halides, s. R. N. Lewis and P. V. Susi, Am. Soc. *74*, 840 (1952).

s. *3*, 682; s. a. E. B. Reid and T. E. Gumpf, J. Org. Chem. *18*, 661 (1953)

Potassium cyanide *KCN*

Carboxylic acids from halides Hal → COOH
Labeled compounds

891. $$R{\cdot}Br \rightarrow [R{\cdot}C^{13}N] \rightarrow R{\cdot}C^{13}OOH$$

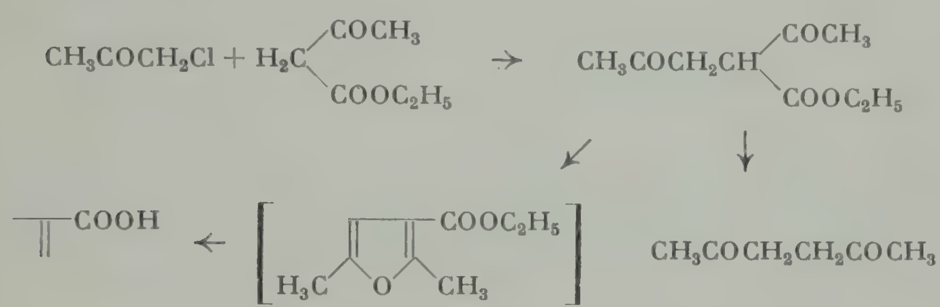
$$CH_3[CH_2]_7CH(OH)CH(OH)[CH_2]_7{\cdot} = R$$

1-Bromo-8,9-dihydroxyheptadecane and $KC^{13}N$ refluxed 48 hrs. in ethanol-water (10:1), KOH added, and refluxing continued for a further 48 hrs. ⟶ dihydroxystearic acid-1-C^{13}. Y: 85%. S. Bergström, K. Pääbo, and M. Rottenberg, Acta Chem. Scand. *6*, 1127 (1952).

Sodium iodide/sodium compound

Synthesis of γ-diketones ←
from β-ketocarboxylic acid esters ←
via β,γ'-diketocarboxylic acid esters
Furans from β-diketones

892.



Sodioacetoacetic ester and a little NaI dissolved at 60-70° in dry acetone, chloroacetone added dropwise with stirring during 20 min., refluxing and stirring continued for 1 hr., acetone distilled off,

and the product isolated → crude α-acetonylacetoacetic ester (Y: 89%) refluxed 75 min. with finely powdered crystalline oxalic acid, and the resulting ester hydrolyzed by refluxing 45 min. with methanolic KOH → 2,5-dimethylfuran-3-carboxylic acid (Y: 91%).—Ring closure occurs also during distillation of α-acetonylacetoacetic ester.

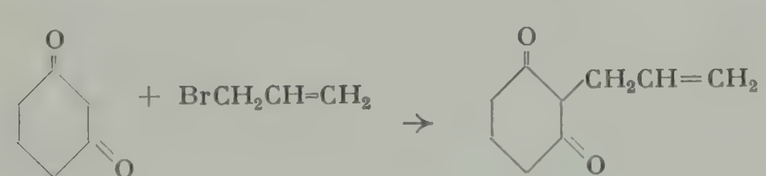
and the resulting mixture of α-acetonylacetoacetic ester and NaCl refluxed 1 hr. with aq. 3%-KOH → acetonylacetone (Y: 65-70%).

O. Dann, H. Distler, and H. Merkel, B. *85*, 457 (1952).

Potassium iodide/potassium hydroxide and copper/potassium hydroxide *KI/KOH and Cu/KOH*

Alkylation of β-diketones CO·CH·CO → CO·CR·CO

893.



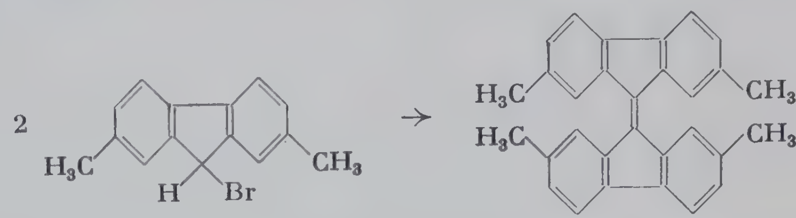
Allyl bromide and Cu-powder added to a soln. of dihydroresorcinol in aq. 20%-KOH, and stirred 5 hrs. at room temp. → 2-allyl-1,3-cyclohexanedione. Y: 75%. F. e., also from chlorides in the presence of KI. s. H. Stetter et al., B. *85*, 1061 (1952); *87*, 1331, 1617 (1954).

Choline $HOCH_2CH_2N(CH_3)_3OH$

Ethylene derivatives from halides by dimerization

2 >CHHal → >C:C<

894.

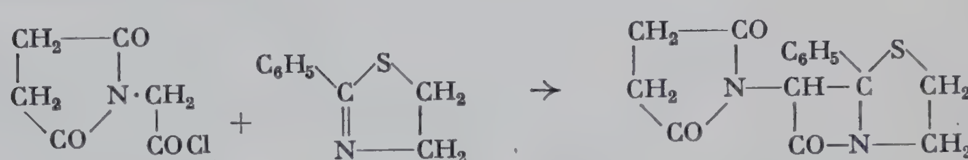


A 50% soln. of choline in methanol added to a soln. of 2,7-dimethyl-9-bromofluorene in acetone, and the product isolated after 30 min. → 2,2′,7,7′-tetramethyl-$\Delta^{9,9'}$-bifluorene. Y: 75.5%. F. e. s. E. D. Bergmann et al., Bl. *1952*, 78.

Triethylamine $(C_2H_5)_3N$

Penicilline ring system

895.

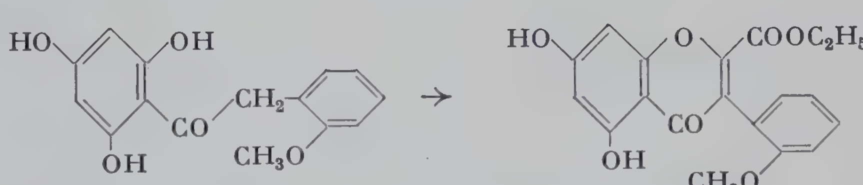


Succinimidoacetyl chloride in methylene chloride added to a soln. of 2-phenyl-2-thiazoline in methylene chloride, stirred rapidly and a dil. soln. of triethylamine in methylene chloride added over a 6 hr. period through a high-dilution cycle (s. Am. Soc. *73*, 4367 (1951)) → 2-phenyl-α-succinimido-2-thiazolidineacetic acid β-lactam. Crude Y: 56%; pure Y: 30%. F. e. s. J. C. Sheehan et al., Am. Soc. *73*, 4376, 4752, 4756 (1951).

Pyridine C_5H_5N

Isoflavones

896.



Ethoxalyl chloride added at 0° with shaking to a soln. of 2-methoxybenzyl 2,4,6-trihydroxyphenyl ketone in pyridine, and the product isolated after 24 hrs. → 2-carbethoxy-5,7-dihydroxy-2′-methoxyisoflavone. Y: 84%. (Soc. *1953*, 1860.)—This method is particularly suited for the preparation of polyhydroxy- and partly alkoxylated hydroxyisoflavones (Soc. *1953*, 1852). W. Baker et al., Soc. *1953*, 1860; f. e. s. Soc. *1953*, 1852.

Copper *Cu*

Diaryls from aryl halides by dimerization 2 ArHal → Ar·Ar

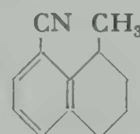
897. cf. Synth. Meth. *1*, 660-2.
Dimethylformamide is a good solvent for this reaction. It offers, however, no advantage with those halides which are inert under the usual conditions. E. s. N. Kornblum and D. L. Kendall, Am. Soc. *74*, 5782 (1952).

Cuprous cyanide *CuCN*

Nitriles from halides Hal → CN

s. *2*, 728; also with $Zn(CN)_2$ s. G. Lock and V. Rieger, B. *86*, 74 (1953)

898.



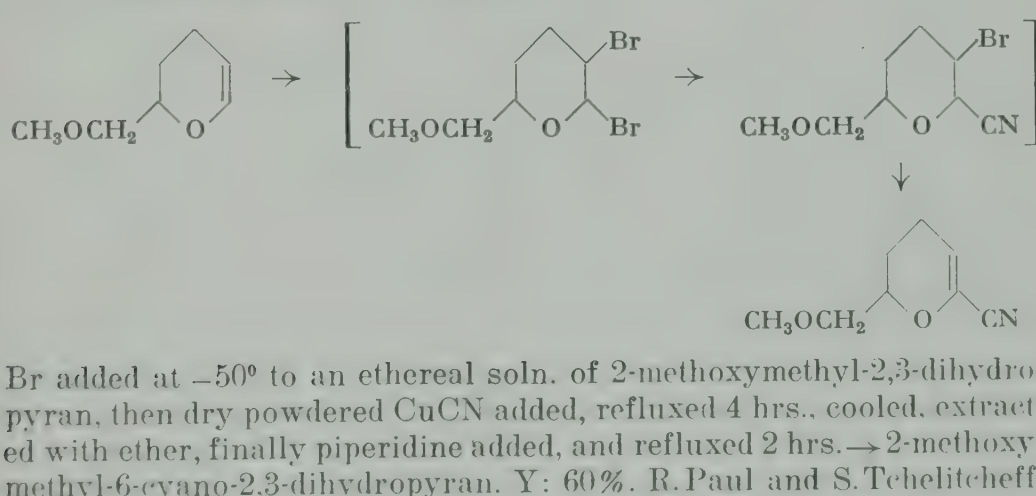
Rosenmund-von Braun nitrile synthesis. A mixture of 0.39 mole 1-methyl-8-chloro-1,2,3,4-tetrahydronaphthalene (prepn. s. 117), 0.44 mole dry CuCN, acetonitrile, and pyridine heated 33 hrs. at 240-250° with shaking → 1-methyl-8-cyano-1,2,3,4-tetrahydronaphthalene. Y: 81%. F. e. s. J. Cason and D. D. Phillips, J. Org. Chem. *17*, 298 (1952); in boiling quinoline s. J. H. Burckhalter et al., Am. Soc. *76*, 4112 (1954).

Carboxylic acids from halides Hal → COOH

s. *8*, 856; furan derivatives s. O. Moldenhauer, G. Trautmann, and R. Pfluger, A. *580*, 188 (1953)

α,β-Ethylenenitriles from ethylene derivatives via 1,2-dibromides and α-bromonitriles C:CH → C:C(CN)

899.



Br added at −50° to an ethereal soln. of 2-methoxymethyl-2,3-dihydropyran, then dry powdered CuCN added, refluxed 4 hrs., cooled, extracted with ether, finally piperidine added, and refluxed 2 hrs. → 2-methoxymethyl-6-cyano-2,3-dihydropyran. Y: 60%. R. Paul and S. Tchelitcheff, Bl. *1952*, 808.

Silver perchlorate — *$AgClO_4$*

Ketones from carboxylic acid chlorides — COCl → COR

s. *7*, 838; s. a. Soc. *1953*, 827

Magnesium — *Mg*

Replacement of alkoxyl by alkyl — OR → R′

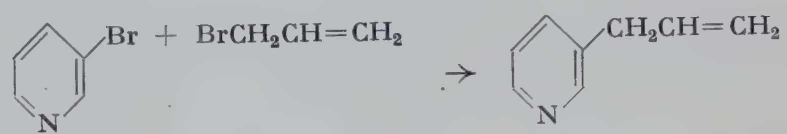
s. *5*, 596; partial replacement s. Am. Soc. *74*, 1624 (1952)

Synthesis of hydrocarbons from halides — RHal + HalR′ → R·R′

900. $(CH_3)_3SiCH(Br)C_6H_5 \rightarrow (CH_3)_3SiCH(MgBr)C_6H_5 + BrCH_2CH{=}CH_2 \rightarrow (CH_3)_3SiCH(CH_2CH{=}CH_2)C_6H_5$

Ethylenesilanes. An ethereal soln. of allyl bromide added to the Grignard reagent from α-bromobenzyltrimethylsilane in ether, and refluxed 4.5 hrs. → 4-trimethylsilyl-4-phenyl-1-butene. Y: 74%. F. e. s. C. R. Hauser and C. R. Hance, Am. Soc. *74*, 5091 (1952).

901.



3-Pyridyl compounds. Allyl bromide added with cooling to an ethereal soln. of 3-pyridyl-MgBr, prepared from 3-bromopyridine and Mg by the entrainment method with the use of ethyl bromide as activator, allowed to stand 12 hrs., then heated for another hr. → 3-(3-pyridyl)propene. Y: 79%. F. e. s. J. P. Wibaut and H. G. P. van der Voort, R. *71*, 798 (1952); methyl iodide as activator s. P. Cagniant, Bl. *1953*, 62.

Selective replacement of chlorine

s. *6*, 806; s. a. O. Riobè, C. r. *236*, 2073 (1953)

Inverse addition of organometallic reagents

s. *9*, 878

Synthesis of hydrocarbons from halides and acoxy compounds — RHal + AcOR′ → R·R′

s. *4*, 781; also hydrogenolysis s. R. C. Fuson et al., Am. Soc. *76*, 499 (1954)

Sec. alcohols from carboxylic acid esters COOR → CH(OH)R′

s. 7, 841: use of isopropyl-MgBr as reducing agent s. O. R. Pierce, J. C. Siegle, and E. T. McBee, Am. Soc. *75*, 6324 (1953)

Synthesis of ethers from acetals $CH(OR)_2 \rightarrow CH(OR)R'$

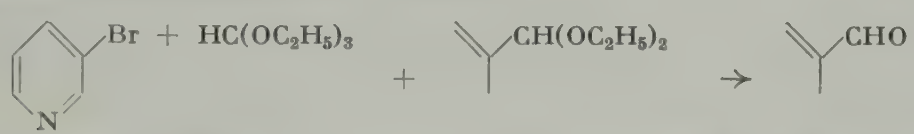
902.

$$(n\text{-}C_4H_9)_2NCH_2CH(OC_2H_5)_2 + BrC_6H_5 \rightarrow (n\text{-}C_4H_9)_2NCH_2CH\begin{cases}OC_2H_5\\C_6H_5\end{cases}$$

N-(Di-n-butyl)aminoacetaldehyde diethylacetal added to ethereal phenyl-MgBr, heated with stirring while most of the ether is removed by distillation, xylene added, distillation continued until the temp. of the reaction mixture reaches 135-140°, then refluxed 4 hrs. with stirring → (β-phenyl-β-ethoxyethyl)di-n-butylamine. Y: 80%.—This method has serious limitations as to yield and purity of product. F. e. s. I. A. Kaye and I. C. Kogon, Am. Soc. *73*, 4893 (1951).

Aldehydes from halides Hal → CHO
via acetals
Synthesis with addition of 1 C-atom

903.



A mixture of 3-bromopyridine and ethyl bromide as activator allowed to react with Mg, the ether replaced by benzene, then ethyl orthoformate added, refluxed 1 hr., then allowed to stand 12 hrs. → nicotinaldehyde diethyl acetal (Y: 50-58%) refluxed 2 hrs. with 10%-HCl under N_2, allowed to stand 12 hrs. at room temp. under N_2, made alkaline with concd. aq. NaOH, and extracted with chloroform → nicotinaldehyde (Y: 82-86%). Over-all Y: 42-49%. F. e., also n-butyl bromide as activator (R. *71*, 798), s. J. P. Wibaut, R. Huls, and H. G. P. van der Voort, R. *71*, 1021, 798 (1952).

Magnesium/alcohol *Mg/C_2H_5OH*

C-Acylation H → COR

904.

$$C_6H_5CH_2COCl + H_2C\begin{cases}COCH_3\\COOC_2H_5\end{cases} \rightarrow C_6H_5CH_2COCH\begin{cases}COCH_3\\COOC_2H_5\end{cases}$$

Mg allowed to react at room temp. with abs. ethanol, the reaction being initiated by addition of a little CCl_4, dry ether added when the reaction subsides, stirred 2-3 hrs. until the reaction stops, acetoacetic ester in dry ether added slowly with ice-cooling and vigorous stirring, then phenacetyl chloride added dropwise with ice-salt cooling and vigorous stirring, which is continued for 1 hr. at room temp., then allowed to stand overnight → α-phenacetylacetoacetic ester. Y: 85%. F. e. s. M. Viscontini et al., Helv. *35*, 2280 (1952); *37*, 41 (1954).

Zinc/acetic anhydride *$Zn/(CH_3CO)_2O$*

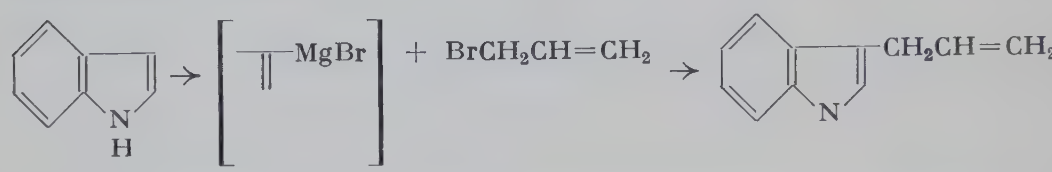
Dimerization of halides 2 RHal → R·R

905. $$2\ n\text{-}C_3F_7I \rightarrow n\text{-}C_6F_{14}$$

A mixture of n-perfluoropropyl iodide, granular Zn, acetic anhydride, and methylene chloride refluxed 24 hrs. at 40-45° → n-perfluorohexane. Y: 77%; conversion: 74%. F. e. s. A. L. Henne et al., Am. Soc. *75*, 5750 (1953).

Alkylmagnesium halide *RMgHal*

Synthesis of hydrocarbons from halides RH + HalR′ → R·R′

906. 

Indole in benzene added slowly with stirring to 20% excess ethereal ethyl-MgBr, stirring continued for 20 min., allyl bromide in benzene added slowly, and stirred overnight at 20° → 3-allylindole. Y: 70%. J. B. Brown, H. B. Henbest, and E. R. H. Jones, Soc. *1952*, 3172.

Cadmium chloride *$CdCl_2$*

Ketones from carboxylic acid chlorides COCl → COR

s. *3*, 694; s. a. M. Renson and R. Huls, Bl. Soc. chim. Belg. *61*, 599 (1952)

Diketodicarboxylic acid esters from dihalides

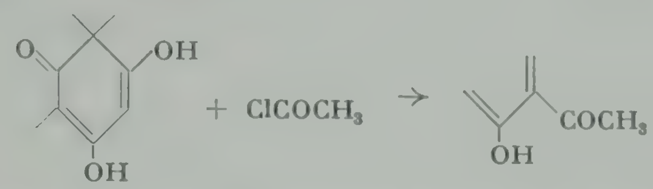
907. $$2\ C_2H_5OOC[CH_2]_4COCl + Br[CH_2]_{10}Br$$
$$\downarrow$$
$$2\ C_2H_5OOC[CH_2]_4CO[CH_2]_{10}CO[CH_2]_4COOC_2H_5$$

10% excess anhydrous $CdCl_2$ added with rapid stirring to a cooled Grignard reagent prepared from 1,10-dibromodecane and Mg in anhydrous ether under N_2 in the presence of a small crystal of iodine, the ice bath removed after 5 min., allowed to warm to room temp. during 10 min., refluxed 45 min. on a steam bath, the ether replaced by benzene, refluxed several min., transferred during 15 min. by means of low pressure N_2 to a rapidly stirred and refluxing soln. of ethyl ω-(chloroformyl)valerate in benzene, refluxed 2 hrs. with stirring, and allowed to stand overnight → diethyl 6,17-diketodocosane-1,22-dioate. Y: 39.1%. F. e. with lower yields s. A. Kreuchunas, Am. Soc. *75*, 3339 (1953).

Aluminum chloride *$AlCl_3$*

Friedel-Crafts ketone syntheses RH → RCOR′

908.



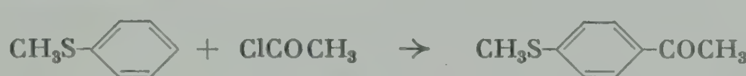
3-Methylfilicinic acid and $AlCl_3$ covered with a layer of CS_2, then nitrobenzene added dropwise, refluxed 15 min., acetyl chloride added, and refluxing continued for 1 hr. → 5-acetyl-3-methylfilicinic acid. Y: 64%. W. Riedl and K. H. Risse, B. *87*, 865 (1954); method s. A. *585*, 38 (1954).

α,β-Ethyleneketones

s. *6*, 814; vinyl ketones s. M. W. Bullock et al., Am. Soc. *76*, 1828 (1954); Q. F. Soper et al., Am. Soc. *76*, 4109 (1954)

Ketothioethers

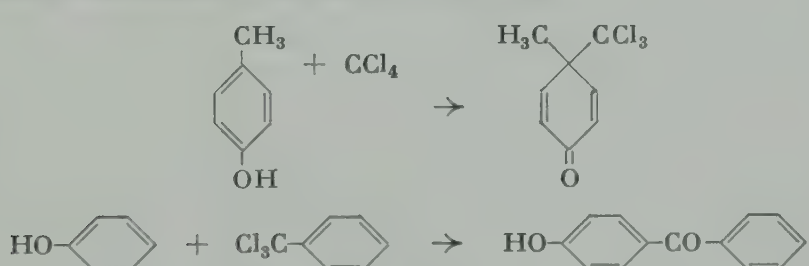
909.



Acetyl chloride added at 0-10° to a well stirred slurry of anhydrous $AlCl_3$ and dry chloroform, then methyl phenyl sulfide added dropwise at 0-5°, the cooling bath removed, stirring continued and the reaction mixture allowed to warm to 20° → p-methylmercaptoacetophenone. Y: 98%. F. e. s. R. A. Cutler, R. J. Stenger, and C. M. Suter, Am. Soc. *74*, 5475 (1952).

Improved Zincke-Suhl synthesis ←
of cyclohexadienones
Synthesis of ketones from 1,1,1-trichlorides

910.



A soln. of p-cresol in CS_2 added dropwise during 10-15 min. to a stirred suspension of $AlCl_3$ in CS_2, then CCl_4 added in one portion, and warmed 2 hrs. at 45° → 4-methyl-4-trichloromethyl-2,5-cyclohexadienone. Y: 60.3%. (J. Org. Chem. *19*, 978.)—Similarly with phenol and benzotrichloride at 0° → p-hydroxybenzophenone. Y: 90.2%. (J. Org. Chem. *19*, 985.) F. e. s. M. S. Newman and A. G. Pinkus, J. Org. Chem. *19*, 978, 985, and f. papers of this series.

Aluminum bromide *$AlBr_3$*

Synthesis of hydrocarbons from bromides $Br \rightarrow R$

911. $$C_6H_5CHBrCHBrCOOH + 2\,C_6H_6 \rightarrow (C_6H_5)_2CH\underset{C_6H_5}{C}HCOOH$$

A soln. of anhydrous $AlBr_3$ in benzene added during 30 min. to a stirred suspension of dibromohydrocinnamic acid in benzene, and refluxed 4 hrs. with stirring $\rightarrow$ α,β,β-triphenylpropionic acid. Y: 66-100%. C. P. Krimmel et al., Org. Synth. *33*, 98 (1953).

Friedel-Crafts ketone syntheses $RH \rightarrow RCOR'$
Ketomercaptans

s. *9*, 655

Stannic chloride *$SnCl_4$*

Darzens synthesis $COCl \rightarrow COR$
Unsatd. ketones from carboxylic acid chlorides

s. *2*, 751; s. a. H. Favre and H. Schinz, Helv. *35*, 2388 (1952); K. W Rosenmund and H. Herzberg, B. *87*, 1581 (1954)

Ferric oxide *Fe_2O_3*

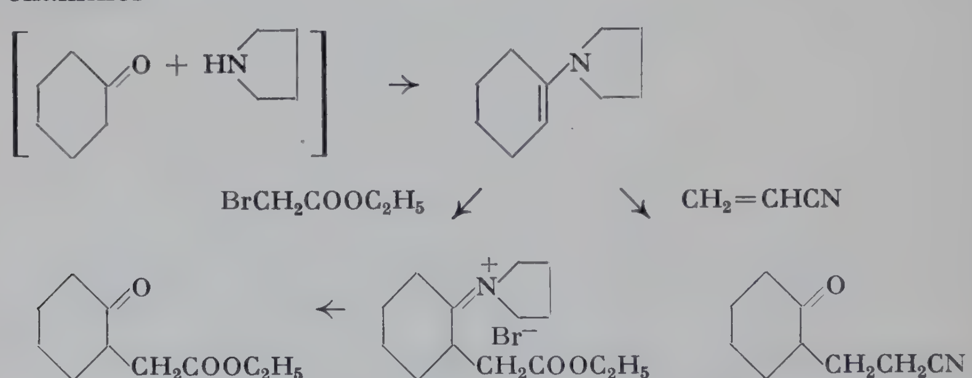
Condensation $RCl + HR' \rightarrow R{\cdot}R'$
with elimination of hydrogen chloride

s. *7*, 856; s. a. J. Org. Chem. *19*, 1529 (1954)

Via intermediates *v.i.*

Substitution of ketones $COCH \rightarrow COCR$
via enamines

912.



Cyclohexenylpyrrolidine allowed to react with

ethyl bromoacetate in methanol, and the resulting quaternary ammonium salt decomposed with water $\rightarrow$ ethyl 2-oxocyclohexaneacetate. Y: good.

acrylonitrile in dioxane $\rightarrow$ 2-cyanoethylcyclohexanone. Y: 80%.

This mild method can be applied to compounds with base sensitive groups. F. e. s. G. Stork, R. Terrell, and J. Szmuszkovicz, Am. Soc. *76*, 2029 (1954).

Sulfur ↑ CC⇸S

Zinc chloride/acetic anhydride $ZnCl_2/(CH_3CO)_2O$

Alkylthiomethylene compounds from orthotrithioformic acid esters C:CHSR

3. $$HC(SC_2H_5)_3 + H_2C(COOC_2H_5)_2 \rightarrow C_2H_5SCH{=}C(COOC_2H_5)_2$$

A mixture of triethyl orthotrithioformate, diethyl malonate, acetic anhydride, and anhydrous $ZnCl_2$ refluxed 10 hrs. at 130-140° → diethyl ethylmercaptomethylenemalonate. Y: 49%. K.-D. Gundermann, A. *578*, 48 (1952).

Carbon ↑ CC⇸C

Electrolysis ↯

Kolbe synthesis $RCOOH + HOOCR' \rightarrow R{\cdot}R'$

s. *1*, 715; s. a. D. G. Bounds, R. P. Linstead, and B. C. L. Weedon, Soc. *1953*, 2393; use of different monoesters of two dicarboxylic acids s. L. Dolejš and L. Novotný, Collection Czechoslov. Chem. Communs. *19*, 716 (1954)

Sodium compound ←

Robinson cyclohexenone ring synthesis ○

s. *1*, 606; cf. A. V. Logan et al., Am. Soc. *76*, 4127 (1945)

Pyridine C_5H_5N

Ketones, also sym., from carboxylic acid anhydrides ←
Selfcondensation of carboxylic acid anhydrides
Decarboxylative acylation

4. $$C_6H_5CH_2COOH + (CH_3CO)_2O \rightarrow C_6H_5CH_2COCH_3$$

A mixture of phenylacetic acid, acetic anhydride, and pyridine refluxed 6 hrs. → phenylacetone. Y: 56%. F. e., also self-condensation of anhydrides to sym. diarylacetones, s. J. A. King and F. H. McMillan, Am. Soc. *73*, 4911 (1951).

Silver salt *Ag⁺*

Hydrocarbons from carboxylic acids by dimerization ←

s. *8*, 873; s. a. R. N. Haszeldine and K. Leedham, Soc. *1953*, 1548

Magnesium oxide *MgO*

Sym. ketones from 2 carboxylic acid molecules 2 RCOOH → RCOR

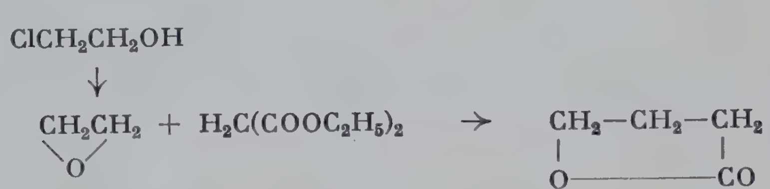
915. $2\ C_{17}H_{35}COOH \rightarrow C_{17}H_{35}COC_{17}H_{35}$

A mixture of stearic acid and MgO heated in a Wood's metal bath at 335-340°, after 1 hr. more stearic acid added in portions during 6 hrs., and heating continued until the total reaction time is 10 hrs. → stearone. Y: 81-87%.—This is a general method for the preparation of higher aliphatic ketones. A. G. Dobson and H. H. Hatt, Org. Synth. *33*, 84 (1953).

Aluminum chloride *$AlCl_3$*

Synthesis of lactones from halogenhydrins via oxido compounds ←

916.



A soln. of malonic ester in abs. chloroform added slowly to $AlCl_3$, then ethylene oxide, generated by dropping ethylene chlorohydrin on powdered NaOH under abs. toluene, passed into the stirred mixture at such a rate as to maintain refluxing, acidified with 5 *N* HCl, and refluxed 5 hrs. → γ-butyrolactone. Y: ca. 100% based on ethylene chlorohydrin consumed. C. Raha, Am. Soc. *75*, 4098 (1953).

Thorium oxide *ThO_2*

Ketones from 2 carboxylic acid molecules ←

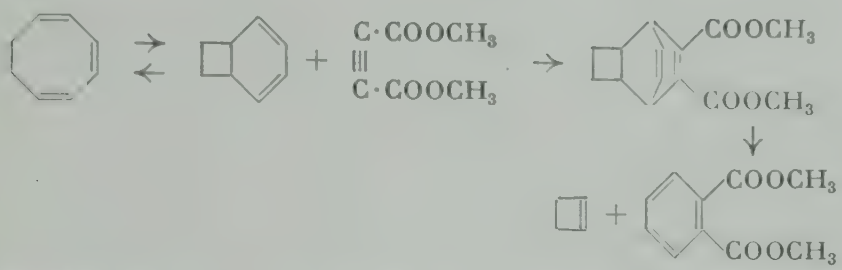
s. *4*, 803; s. a. G. Weitzel and J. Wojahn, H. *287*, 296 (1951)

Via intermediates *v.i.*

Sym. ketones from carboxylic acid chlorides via ketene dimers 2 RCOCl → RCOR

s. *7*, 862; sym. keto-α,ω-dicarboxylic acids s. A. T. Blomquist et al., Am. Soc. *74*, 4203 (1952)

Acetylenedicarboxylic acid esters synthesis ←
Alder-Rickert synthesis
Valence tautomerism

17. 

1,3,5-Cycloöctatriene regenerated from the Ag-nitrate complex with aq. NH_3, taken up in benzene, dried over silica gel, added to dimethyl acetylenedicarboxylate, and warmed 24 hrs. at 60° under N_2 → adduct (Y: 77%) heated 20 min. under N_2 200°/100 mm. → cyclobutene (Y: 95%) and dimethyl phthalate.—1,3,5-Cycloöctatriene is in mobile equilibrium with bicyclo[4.2.0]octa-2,4-diene. A. C. Cope et al., Am. Soc. *74*, 4867 (1952).

Elimination

Hydrogen ↑ CC ⇑ H

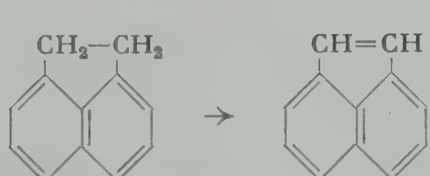
Calcined magnesite *MgO*

α,β-Ethylenearenes by dehydrogenation CHCH → C:C

18. Ethylnaphthalene (ca. 50:50 mixture of α- and β-isomers) passed at 600°/100 mm over calcined magnesite for 3 hrs. with a contact time of 1 sec. → vinylnaphthalene. Y per pass: 44.7%; ultimate Y: 90.3%.—In general, the yield is benefited by low temp., low pressure, short contact time, and high ratio of diluent to startg. m. in the feed stock. Steam is superior to benzene as diluent because of the greater ease of final separation. F. catalysts s. J. E. Nickels and B. B. Corson, Ind. Eng. Chem. *43*, 1685 (1951).

Zinc oxide-alumina-calcium oxide *ZnO,Al_2O_3,CaO*

Dehydrogenation in the vapor phase

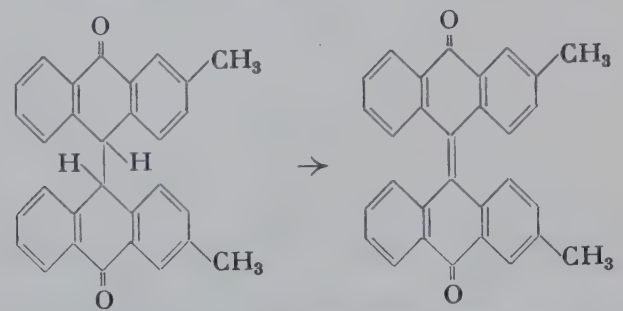
19. 

A mixture of acenapthene and steam as diluent passed at ca. 600-650° through a ZnO,Al_2O_3,CaO-catalyst → acenaphthylene. Y: 90%; purity

up to 98%. M. Kaufman and A. F. Williams, J. Applied Chem. *1*, 489 (1951).

Quinones ←

Bianthrones from bianthronyls

920. 

2,2′-Dimethylbianthronyl enolized by refluxing with anhydrous alc. KOH for 10 min., filtered, poured into a mixture of ice and concd. HCl, filtered, the residue dissolved in acetone, p-benzoquinone in acetone added, and kept 12 hrs. in the dark → 2,2′-dimethylbianthrone. Y: 90%. F. e. s. E.D. Bergmann and E. Loewenthal, Bl. *1952*, 66; Soc. *1953*, 2572.

Chloranil ←

Dehydrogenation

921. Of several quinones tested as dehydrogenation agents, chloranil seems to be the most suitable. N. Dost, R. *71*, 857 (1952); s. a. J. Swidinsky, F. H. McMillan, and J. A. King, Am. Soc. *76*, 1148 (1954).

Oxygen/potassium hydroxide O_2/KOH

to quinones

s. *3*, 705; s. a. E. A. Braude, J. S. Fawcett, and A. A. Webb, Soc. *1954*, 1049

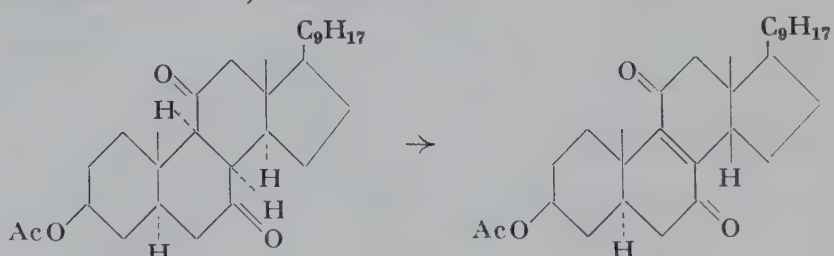
Sulfur *S*

Aromatization

s. *9*, 923

Selenium dioxide SeO_2

Ene-1,4-diones from 1,4-diketones

922. 

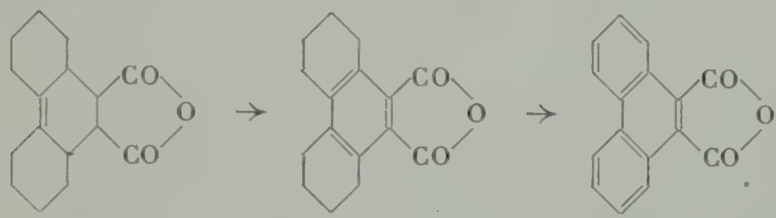
7,11-Diketo-8α-ergost-22-en-3β-yl acetate refluxed 30 min. with SeO_2 in abs. alcohol → 7,11-diketoergosta-8.22-dien-3β-yl acetate. Y: excellent.—

Ready conversion requires a *cis*-relation for the eliminated H-atoms. C. S. Barnes and D. H. R. Barton, Soc. *1953*, 1419.

Bromine *Br*

Stepwise aromatization
Phenanthrene derivatives

23.



Br in a little acetic acid added to a soln. of dodecahydrophenanthrene-9,10-dicarboxylic acid anhydride in glacial acetic acid, allowed to stand 24 hrs., the precipitated product separated (Y: 56.3%), and a further quantity obtained by passing a vigorous N_2-stream through the boiling mother liquor for 16 hrs. to remove HBr → 1,2,3,4,5,6,7,8-octahydrophenanthrene-9,10-dicarboxylic acid anhydride (over-all Y: 78.3%) heated 20 min. with S at 300-330° in a metal bath → phenanthrene-9,10-dicarboxylic acid anhydride (Y: 77.6%). Over-all Y: 60%. P. Lambert and R. H. Martin, Bull. soc. chim. Belges *61*, 513 (1952).

Dehydrogenation

of (o-di-N)-heterocyclics

s. *6*, 835; pyrazoles s. W. E. Parham and W. R. Hasek, Am. Soc. *76*, 799 (1954); pyridazones in acetic acid s. *7*, 866; s. a. E. A. Steck, R. P. Brundage, and L. T. Fletcher, Am. Soc. *75*, 1117 (1953)

Palladium-carbon *Pd-C*

s. *9*, 859, 931

Azulenes

s. *2*, 612, 764; *9*, 859; s. a. H. Pommer, A. *579*, 47 (1953)

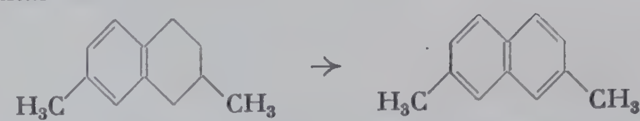
Palladium-carbon-magnesium oxide *Pd-C-MgO*

24.

1.2,3.4,5.6-Hexahydroazulene passed at 320-330° through a catalyst of 5%-Pd-charcoal suspended on 40% MgO and 60% Norite, in a special apparatus (s. original) → azulene. Y: 32%. A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, Am. Soc. *75*, 4980 (1953).

Palladium,platinum-carbon *Pd,Pt-C*

925.



in the vapor phase. 2,7-Dimethyltetrahydronaphthalene allowed to react at 440° with a charcoal catalyst containing 0.5% each of Pd and Pt → 2,7-dimethylnaphthalene. Y: 86%. W. Baker, J. F. W. McOmie, and W. K. Warburton, Soc. *1952*, 2991.

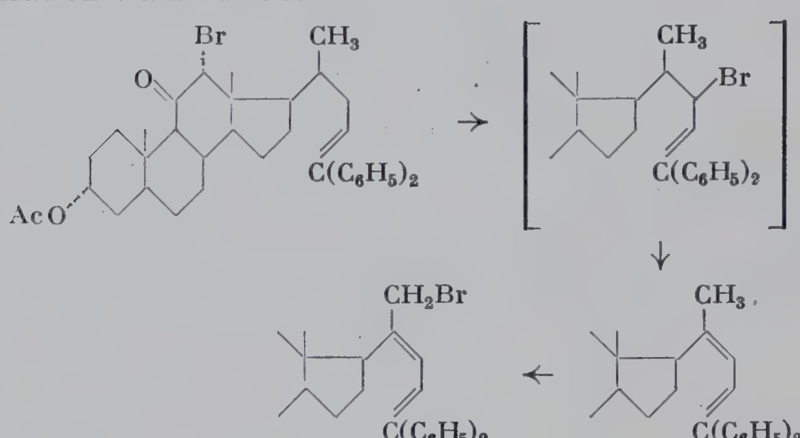
926.

A 2% soln. of decahydroazulene in decalin passed at ca. 380° through a Pyrex tube filled with a Pd-Pt-charcoal catalyst → azulene. Y: 24%.— The yield could be improved by the use of a large amount of *decalin as carrier.* W. Baker, W. K. Warburton, and L. J. Breddy, Soc. *1953*, 4149.

Via intermediates *v.i.*

β,γ-Ethylenebromides from hydrocarbons ←
Dehydration via bromides

927.



3α-acetoxy-11-keto-12-bromo-24,24-diphenyl-Δ^{23}-cholene

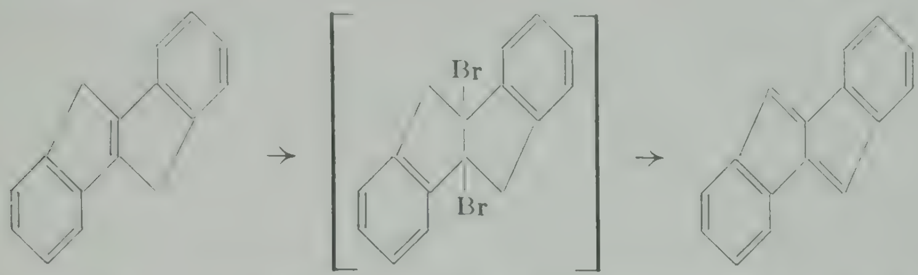
A soln. of 3α-acetoxy-11-keto-12-bromo-24,24-diphenyl-Δ^{23}-cholene in allyl bromide stirred and gently refluxed while treated with 2.2 molar equivalents of N-bromosuccinimide, and the product isolated after 12 min. → 3α-acetoxy-11-keto-12,21-dibromo-24,24-diphenyl-$\Delta^{20,22;23}$-choladiene (startg. m. f. 699). Y: at least 70%.

A mixture of 3α-acetoxy-11-keto-12-bromo-24,24-diphenyl-Δ^{23}-cholene and ca. 1 molar equivalent of N-bromosuccinimide in CCl_4 boiled 8 min. over a 500 Watt lamp, evaporated in vacuo, then boiled 10 min. in allyl bromide → 3α-acetoxy-11-keto-12-bromo-24,24-diphenyl-$\Delta^{20,22;23}$-choladiene (400 mg. from 620 mg.).

J. Heer and A. Wettstein, Helv. *36*, 891 (1953).

Dehydrogenation CHCH → C:C

8.



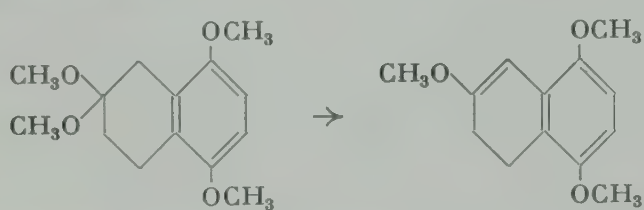
Bromine in CS_2 added dropwise at 0° during 1 min. to a soln. of 3,6-dihydrodibenzopentalene in CS_2, a rapid stream of N_2 bubbled through the liquid until no more HBr is evolved, the solvent distilled off in vacuo, the residue dissolved in dry benzene, Ag-acetate added, and the suspension refluxed 2 hrs. → 1,2:4,5-dibenzopentalene. Y: 59%. C. T. Blood and R. P. Linstead, Soc. *1952*, 2263.

Oxygen ↑ CC ⇑ O

Without additional reagents *w.a.r.*

Enolethers from acetals CHC(OR)$_2$ → C:C(OR)

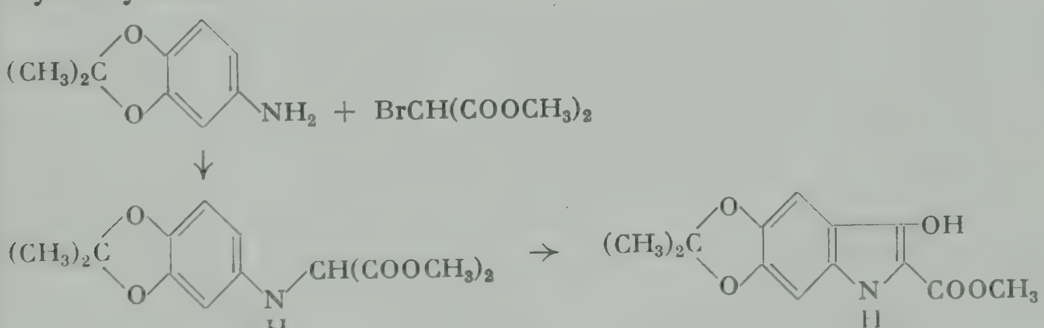
9.



3.7 g. 5,8-dimethoxy-2-keto-1,2,3,4-tetrahydrophthalene dimethyl ketal refluxed 2 hrs. in abs. xylene → 3.4 g. 1,4,6-trimethoxy-7,8-dihydronaphthalene. C. A. Grob and W. Jundt, Helv. *35*, 2111 (1952).

Hydroxyindoles ○

0.



A mixture of isopropylidene-3,4-dihydroxyaniline and dimethyl bromomalonate refluxed 4 hrs. in benzene → dimethyl (isopropylidene-3,4-dihydroxyanilido)malonate (Y: 72%) added at 240-245° during 10 min. to paraffin oil → methyl isopropylidene-5,6-dihydroxyindoxyl-2-carboxylate (Y: 74%). R. W. Balsiger et al., Helv. *36*, 708 (1953).

Phenanthrolines
EMME method

s. *3*, 715; s. a. A. R. Surrey and R. A. Cutler, Am. Soc. *76*, 1109 (1954)

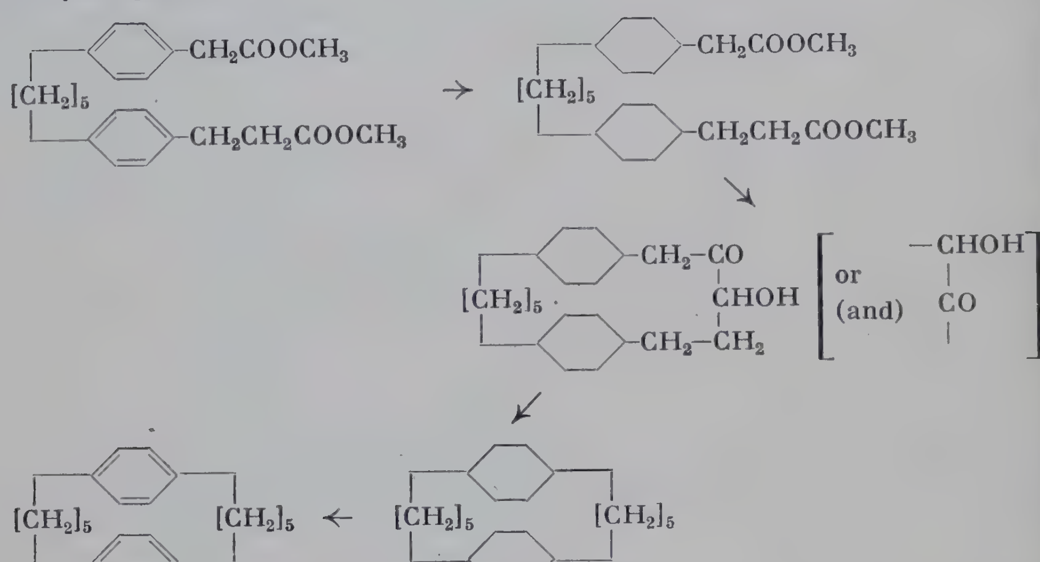
Sodium *Na*

Acyloin condensation –CH(OH)CO–

s. *4*, 816; s. a. A. T. Blomquist and Liang Huang Liu, Am. Soc. 75, 2153 (1953)

Paracyclophanes
Hydrogenation of benzene rings
Acyloin condensation
Hydrocarbons from acyloins
Dehydrogenation

931.



p-Carbomethoxymethyl-p′-(β-carbomethoxyethyl)-1,5-diphenylpentane hydrogenated in acetic acid with PtO_2 at 25° and atmospheric pressure → p-carbomethoxymethyl-p′-(β-carbomethoxyethyl)-1,5-dicyclohexylpentane (Y: 88%) in xylene added during 12 hrs. to Na in xylene (apparatus with high speed stirrer, and high dilution technique s. Am. Soc. *73*, 5691 (1951)), then heated an additional hr. → crude 2(3)-hydroxy-3(2)-keto-p,p′-pentamethylene-1,5-dicyclohexylpentane (Y: 62%) added along with concd. HCl and acetic acid to Zn-amalgam, refluxed 40 hrs. with addition of more concd. HCl at 12-hr. intervals and the crude product containing olefins hydrogenated with PtO_2 in acetic acid-ethyl acetate → diastereomeric mixture of p-p′-pentamethylene-1,5-dicyclohexylpentanes (Y: 76%) heated with 10%-Pd-on-charcoal at 240-320° for 1.5 hrs. → p,p′-pentamethylene-1,5-diphenylpentane (Y: 96%).— Ring closure can be achieved only when the benzene rings are hydrogenated. F. e. s. N. L. Allinger and D. J. Cram, Am. Soc. *76*, 2362 (1954).

Sodium hydride *NaH*

Dieckmann condensation ○
Cyclic β-diketones

s. *8*, 885; s. a. H. Conroy, Am. Soc. *74*, 3046 (1952)

Potassium hydroxide *KOH*

Partial dehydration CHC(OH) → C:C

s. *9*, 239

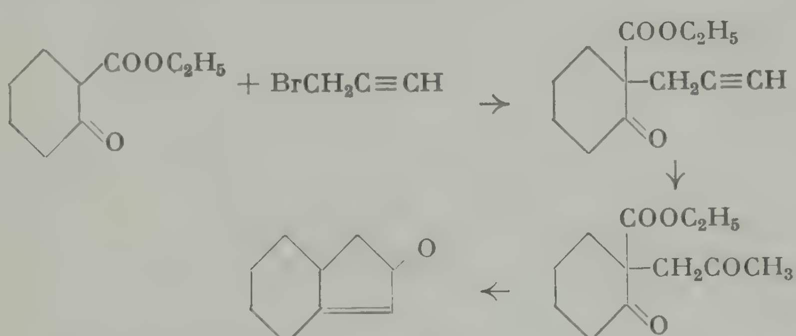
Elimination reaction of esters ←
α,β-Ethylenecarboxylic acid esters
from β-acoxycarboxylic acid esters

32. $$\underset{\displaystyle ONO_2}{CH_3CHCH_2COOCH_3} \rightarrow CH_3CH{=}CHCOOH$$

β-Acoxyesters can be dehydrated by alkali under conditions where the parent β-hydroxyesters do not give this reaction. The proportion of elimination to hydrolysis at the β-C atom increases with the strength of the acid of the β-acoxy group. The proportion of elimination is also greater when the resulting unsatd. acid is highly conjugated.—E: Methyl β-nitroxybutyrate and KOH in doxane-water refluxed 2 hrs. → crotonic acid. Y: 80%. F. e. s. R. P. Linstead, L. N. Owen, and R. F. Webb. Soc. *1953*, 1211; elimination reactions of esters s. a. the following papers of this series.

Cycloalkenone ring from diketones ○
with simultaneous decarbalkoxylation
Alkylation of β-ketocarboxylic acid esters
Ketones from acetylene derivatives

33.



A mixture of Na-ethoxide soln. and ethyl 2-ketocyclohexane-1-carboxylate refluxed 30 min., propargyl bromide added to the boiling soln. during 1 hr., and heating continued for 2 hrs. → ethyl 2-keto-1-propargylcyclohexane-1-carboxylate (Y: 83%) dissolved in methanol, added slowly to a catalyst soln. prepared by warming together red HgO, FB_3-ether complex, trichloroacetic acid, and methanol, and shaken 2

hrs. at room temp. after the exothermic reaction has ceased → ethyl 1-acetonyl-2-ketocyclohexane-1-carboxylate (Y: 75%) refluxed 6 hrs. with aq. 5%-KOH under N_2, cooled, acidified with dil. H_2SO_4, extracted with ether, evaporated, and distilled → bicyclo[4.3.0]-6-nonen-8-one (Y: 73%). A. M. Islam and R. A. Raphael, Soc. *1952*, 4086; ring closure s. a. Soc. *1953*, 3718.

Ethylene derivatives from sulfonic acid esters Hydrolytic ring opening of isocyclics ←

s. *9*, 772

Potassium hydroxide/alcohol

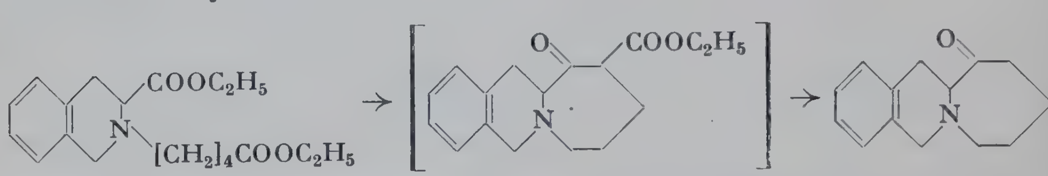
Cyclohexenone ring from enollactones via enollactols

s. *8*, 884; s. a. L. B. Barkley et al., Am. Soc. *76*, 5014 (1954)

Potassium-tert-butoxide *KOR*

Dieckmann cyclization ○

934.

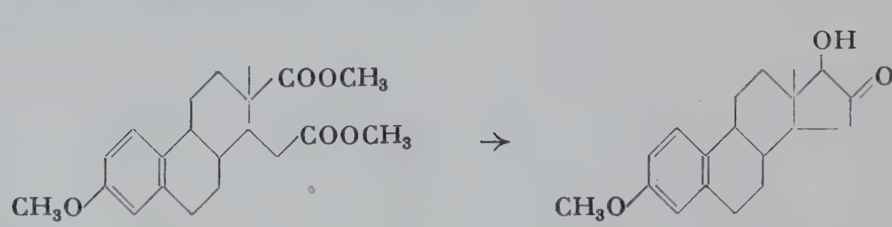


A soln. of ethyl N-(δ-carbethoxybutyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate in xylene added during 17 hrs. under N_2 with stirring at reflux temp. to K-*tert*-butoxide in xylene, with periodical removal of the alcohol formed, then poured into 6 *N* HCl, heated 12 hrs. with stirring on a steam bath until the $FeCl_3$-test is negative, the HCl-layer separated from the xylene layer and concentrated in vacuo → benzo[i]-6-keto-1-azabicyclo[5.4.0]hendecane. Y: 69%. F. e. s. N. J. Leonard et al., Am. Soc. *76*, 3193 (1954); also high dilution apparatus s. Am. Soc. *74*, 1704 (1952).

Sodium/liq. ammonia *Na/NH₃*

Stereospecific acyloin condensation ⌐CH(OH)—CO⌐

935.



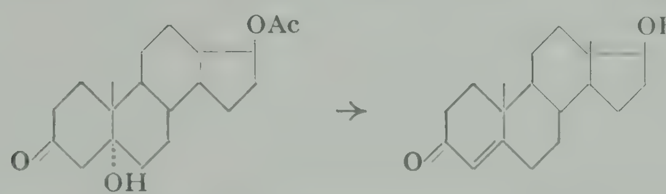
A soln. of dimethyl marrianolate methyl ether in dry ether added during 1.5 hrs. with efficient stirring under N_2 to a soln. of Na in liq.

NH_3-ether, stirring continued as the flask is allowed to come slowly to room temp. in a slow N_2-stream, and the product isolated after 4 hrs. → 16-keto-17β-estradiol-3-methyl ether. Y: 96%. J. C. Sheehan, R. A. Coderre, and P. A. Cruickshank, Am. Soc. 75, 6231 (1953).

Potassium carbonate *K_2CO_3*

α,β-Ethyleneketones from β-hydroxyketones CHC(OH) → C:C

936.



3-Keto-5-hydroxysteroids are as β-hydroxyketones easily dehydrated in alkaline medium.—E: 40 mg. 3-keto-5-hydroxy-17β-acetoxyandrostane allowed to stand 5 days at room temp. in methanol-water containing K-carbonate → 20 mg. testosterone. F. e. s. S. A. Julia, P. A. Plattner, and H. Heusser, Helv. *35*, 665 (1952).

Pyridine with P_2O_5, PBr_3, $POCl_3$, $SOCl_2$ *C_5H_5N*

s. under the latter reagents

Collidine ←

Ethylene derivatives from tosylates CHC(OTs) → C:C

s. *2*, 805; s. a. G. Rosenkranz, O. Mancera, and F. Sondheimer, Am. Soc. *76*, 2227 (1954)

Cupric sulfate *$CuSO_4$*

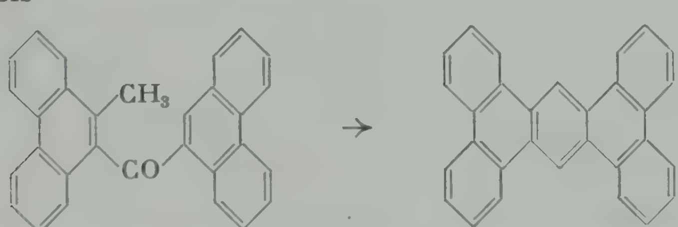
Dehydration of alcohols CHC(OH) → C:C

s. *8*, 889; s. a. M. J. Schlatter, Am. Soc. *76*, 4952 (1954)

Zinc *Zn*

Isocyclics from ketones ○
Elbs pyrolysis

937.



A mixture of 10-methyl-9-phenanthryl 9-phenanthryl ketone and Zn-powder heated 30 min. at 400-410° → tetrabenz[a,c,h,j]anthracene (startg. m. f. 254). Y: 47%. P. Lambert and R. H. Martin, Bull. soc. chim. Belges *61*, 124 (1952).

Methylmagnesium bromide CH_3MgBr

Ethylene derivatives from sulfonic acid esters ←
Hydrolytic ring opening of isocyclics

s. *9*, 772

Zinc chloride $ZnCl_2$

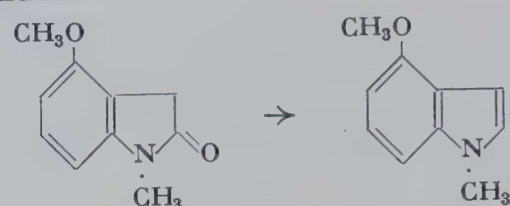
N-Heterocyclics from ○
hydroxycarboxylic acid amides

s. *9*, 956

Lithium aluminum hydride $LiAlH_4$

Indoles from oxindoles

938.



A suspension of 5 g. 4-methoxy-1-methyloxindole in dry ether stirred and treated portionwise during 20 min. with $LiAlH_4$, and stirring continued for 20 min. → 3 g. 4-methoxy-1-methylindole and 0.5 g. startg. m. J. W. Cook, J. D. Loudon, and P. McCloskey, Soc. *1952*, 3904.

Boric acid HBO_2

Anthraquinone ring closure

s. *5*, 481; s. a. G. Wolf, Am. Soc. *75*, 2673 (1953)

Alumina Al_2O_3

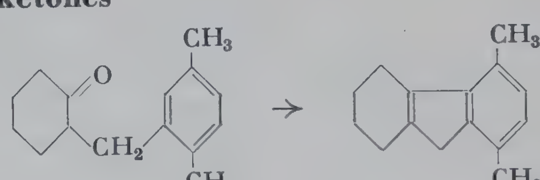
Dehydration of alcohols CHC(OH) → C:C

s. *9*, 981

Aluminum chloride $AlCl_3$

Cyclodehydration
Isocyclics from ketones

939.

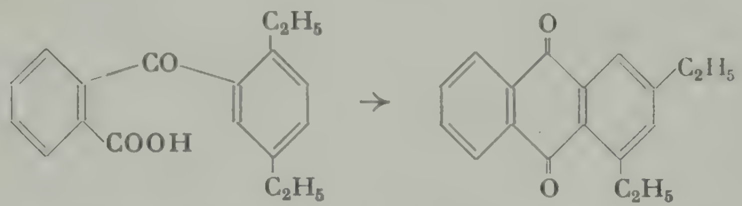


3.1 moles $AlCl_3$ added to a soln. of 2-(2′,5′-dimethylbenzyl)cyclohexanone in petroleum ether, and heated ca. 4 hrs. on a water bath with stirring until the HCl-evolution ceases → 1,4-dimethyl-5,6,7,8-tetrahydrofluorene. Y: 65%. F. e., with lower yields, s. J. Colonge and J. Sibeud, Bl. *1953*, 75.

Aluminum chloride/sodium chloride *$AlCl_3/NaCl$*

Anthraquinones
Alkyl migration

40.



o-(2,5-Diethylbenzoyl)benzoic acid, $AlCl_3$, and NaCl powdered together, then heated 2 hrs. at 160° → 1,3-diethylanthraquinone. Y: 90%. F. e., also without migration. s. G. Baddeley, G. Holt, and S. M. Makar, Soc *1952*, 2415.

Carbon *C*

Ketenes from carboxylic acid anhydrides $(RCH_2CO)_2O \rightarrow 2\,RCH{:}C{:}O$

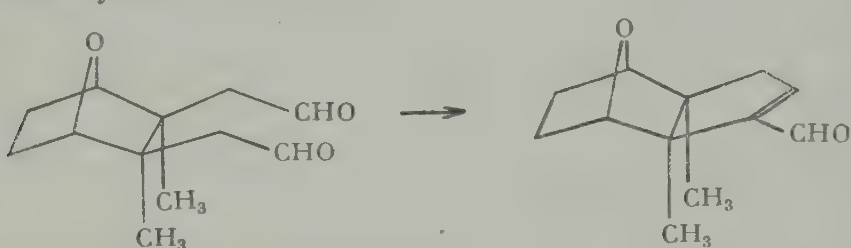
41. $$(CH_3CH_2CO)_2O \rightarrow 2\ CH_3CH{=}C{=}O$$

Propionic anhydride dropped at ca. 150° into a flask and the vapor passed through a quartz tube, having a thin carbon coating over the inner surface, at ca. 550°/5 mm. and a contact time of ca. 10^{-2} sec. → methylketene. Conversion up to 90%. Y: 90%. A. D. Jenkins, Soc. *1952*, 2563.

Piperidinium acetate ←

Cyclic α,β-ethylenealdehydes from dialdehydes ○

42.



Piperidine acetate in benzene added with stirring under N_2 to a soln. of dialdehyde in benzene, and warmed 1 hr. at 60-70° → *exo*-1-formyl-4,7-epoxy-8,9-*cis*-dimethyl-4,5,6,7,8,9-hexahydroindene. Y: 75%. G. Stork et al., Am. Soc. *75*, 384 (1953).

Acetic anhydride *$(CH_3CO)_2O$*

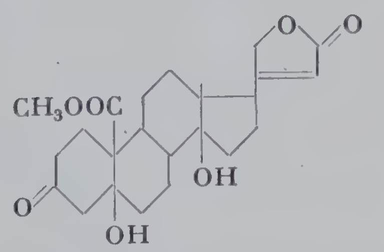
Ring closure with acetic anhydride

43. cf. Synth. Meth. *2*, 776/7
Anthrones were obtained directly instead of the expected anthranol acetates by J. Cason and D. D. Phillips, J. Org. Chem. *17*, 298 (1952).

Acetic acid *CH_3COOH*

Partial dehydration CHC(OH) → C:C

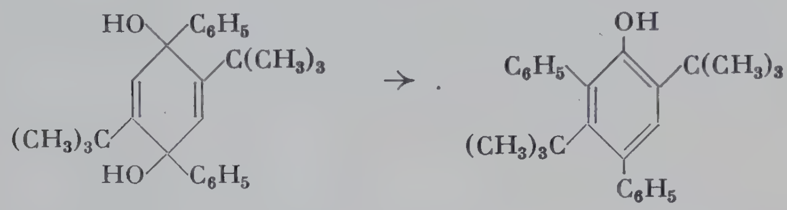
944.



A soln. of 3 g. methyl strophanthidon-19-ate in glacial acetic acid heated 10 min. at an oil bath temp. of 125° → 2.1 g. methyl 5-anhydrostrophanthidon-19-ate. A. Stoll, A. von Wartburg, and J. Renz, Helv. *36*, 1557 (1953).

Phenols by dehydration with rearrangement ←

945.



2,5-Di-t-butyl-1,4-diphenyl-2,5-cyclohexadiene-1,4-diol refluxed 2 hrs. with glacial acetic acid → 2,4-diphenyl-3,6-di-t-butylphenol. Y: ca. 100%. H. M. Crawford, M. Lumpkin, and M. McDonald, Am. Soc. *74*, 4087 (1952).

Dienes from alkoxyethylene derivatives ←

s. *9*, 950

Stannic chloride/phosphorus pentachloride *$SnCl_4/PCl_5$*
s. Phosphorus pentachloride/stannic chloride

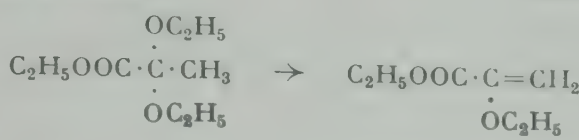
Phosphorus pentoxide *P_2O_5*

3,4-Dihydroisoquinolines ○

s. *5*, 621; s. a. A. R. Battersby, H. T. Openshaw, and H. C. S. Wood, Soc. *1953*, 2463

Phosphorus pentoxide/pyridine *P_2O_5/C_5H_5N*

Enolethers from acetals $CHC(OR)_2 \rightarrow C{:}C(OR)$

946.


P_2O_5 added to a soln. of ethyl α,α-diethoxypropionate in pyridine, and refluxed 2 hrs. → ethyl α-ethoxyacrylate. Y: 85%. C. L. Stevens and A. E. Sherr, J. Org. Chem. *17*, 1177 (1952).

Polyphosphoric acid *$H(PO_3H)_xOH$*

Cyclization ○

s. a. *8*, 899; s. a. F. Uhlig, Ang. Ch. *66*, 435 (1954)

Isocyclics from oxo compounds

from ketones s. *8*, 899; also from aldehydes s. J. Koo and J. L. Hartwell, Am. Soc. *75*, 1625, 1889 (1953)

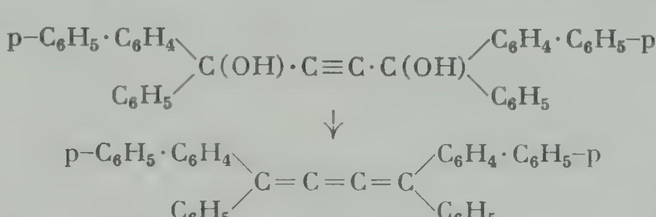
Cyclic ketones from carboxylic acids

947. cf. Synth. Meth. *6*, 854

Temp. and time of reaction have to be carefully controlled to obtain an optimum yield. E. s. H. Schmid and M. Burger, Helv. *35*, 928 (1952).

Phosphorus tribromide/pyridine *PBr_3/C_5H_5N*

1,2,3-Trienes from 2-acetylene-1,4-diols $C(OH){\cdot}C{\equiv}C{\cdot}C(OH) \rightarrow C{=}C{=}C{=}C$

948.


PBr_3 in pyridine added with shaking and cooling to a soln. of 1,4-diphenyl-1,4-dibiphenyl-2-butin-1,4-diol in pyridine, after 5 min. some alcohol cautiously added followed by water, and the product isolated after several hrs. → 1,4-diphenyl-1,4-dibiphenylbutatriene. Y: 64%. F. e., with lower yields, s. R. Kuhn and J. Jahn, B. *86*, 759 (1953).

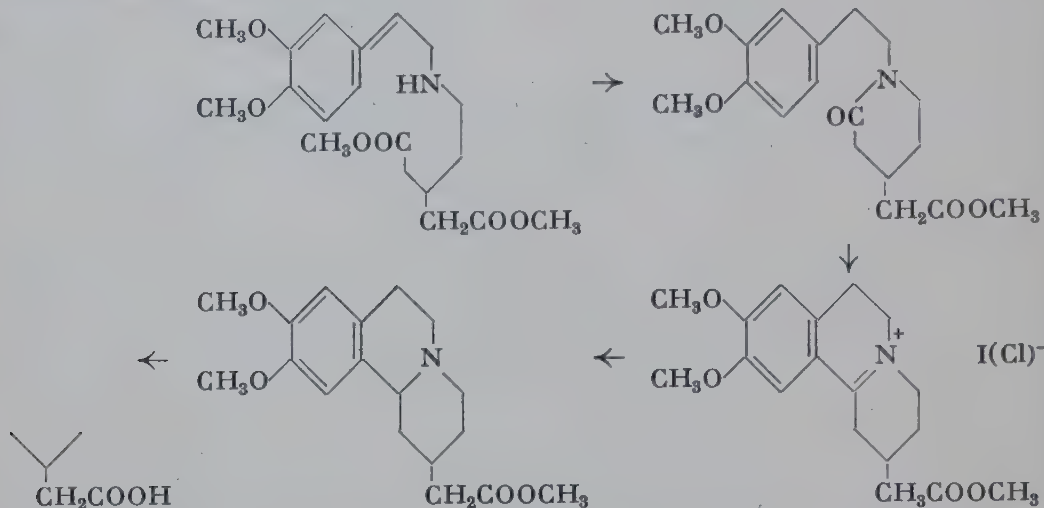
Phosphorus oxychloride *$POCl_3$*

Bischler-Napieralski ring closure ○
3,4-Dihydroisoquinolines

s. *2*, 788; s. a. A. M. Barbier and P. Rumpf, Bl. *1953*, 293

Benzo[a]quinolizine ring
Lactam ring closure
Tert. amines from
quaternary ammonium salts

949.



10.2 g. dimethyl β-(2-homoveratrylaminoethyl)glutarate heated 2 hrs. at 190-200°/1 mm. → 7.2 g. methyl 1-(3,4-dimethoxyphenethyl)-2-oxo-4-piperidineacetate, 0.75 g. dissolved in toluene, treated with $POCl_3$, refluxed several min., evaporated in vacuo, the residue dissolved in a little water, buffered with Na-acetate, and treated with concd. HI soln. → 0.98 g. 2-(carbomethoxymethyl)-1,2,3,4,6,7-hexahydro-9,10-dimethoxybenzo[a]quinolizinium iodide, 12.8 g. treated repeatedly with AgCl in water, hydrogenated with PtO_2 at 18° for 2 hrs., and hydrolyzed by boiling with 5%-HCl for 1 hr. → 9.2 g. 2-(carboxymethyl)-1,2,3,4,6,7-hexahydro-9,10-dimethoxy-11bH-benzo[a]quinolizine hydrochloride. M. Pailer and H. Strohmayer, M. *83*, 1198 (1952).

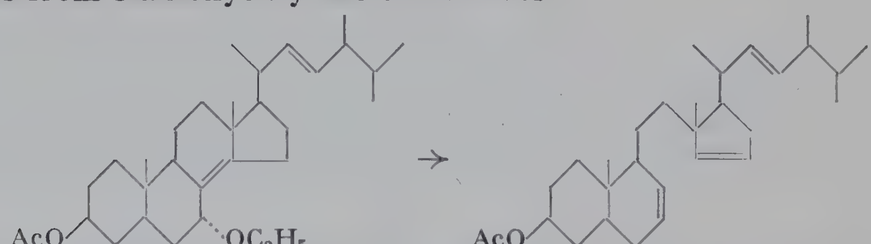
Phosphorus oxychloride/pyridine *$POCl_3/C_5H_5N$*

Dehydration of alcohols CHC(OH) → C:C

s. 7, 883; s. a. W. Oroshnik and A. D. Mebane, Am. Soc. *76*, 5719 (1954)

Dienes from 3-alkoxyethylene derivatives ←

950.



A soln. of 3β-acetoxy-7α-ethoxy-$\Delta^{8(14),22}$-ergostadiene in benzene-pyridine treated at 0° with $POCl_3$ in benzene and let stand overnight at 25° → ergosterol-B_3 acetate. Crude Y: 80%. Also with acetic acid s. L. F. Fieser and G. Ourisson, Am. Soc. *75*, 4404 (1953).

Phosphorus pentachloride *PCl_5*

Bischler-Napieralski isoquinoline ring closure ○

s. *2*, 793; s. a. M. B. Moore et al., Am. Soc. *76*, 3656 (1954)

Dehydration with ring contraction ←

s. *8*, 901; s. a. D. H. R. Barton, D. A. J. Ives and B. R. Thomas. Soc. *1954*, 903

Phosphorus pentachloride/stannic chloride *$PCl_5/SnCl_4$*

Cyclic ketones from carboxylic acids ○

s. *7*, 325; s. a. P. Cagniant, Bl. *1952*, 970

Thionyl chloride/pyridine *$SOCl_2/C_5C_5N$*

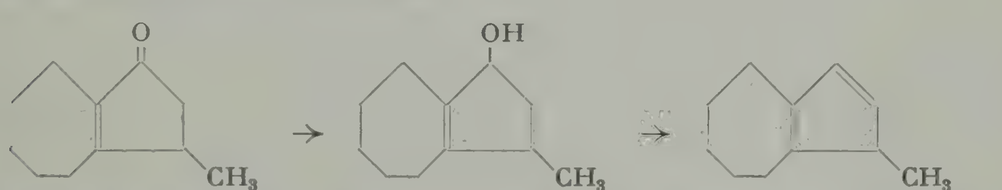
Dehydration of alcohols CHC(OH) → C:C

s. *7*, 239; s. a. Soc. *1954*, 1226

Potassium hydrogen sulfate *$KHSO_4$*

Ethylene derivatives from ketones via sec. alcohols

951.

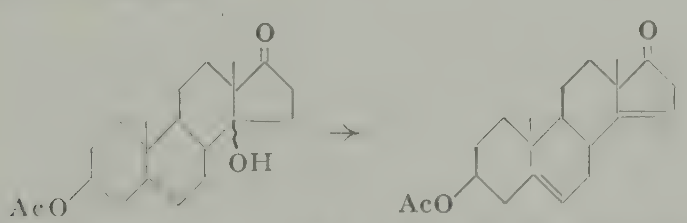


Δ^9-Octahydro-1-keto-3-methylazulene reduced with $LiAlH_4$ in ether at 0° → Δ^9-octahydro-1-hydroxy-3-methylazulene (Y: 83%) mixed with $KHSO_4$ and rapidly distilled at ca. 0.5 mm → 1,4,5,6,7,8-hexahydro-1-methylazulene (Y: 84%). F. e. s. E. A. Braude and W. F. Forbes, Soc. *1953*, 2208.

Potassium hydrogen sulfate/acetic anhydride *$KHSO_4/(CH_3CO)_2O$*

Dehydration of alcohols

952.



Fused $KHSO_4$ added to a soln. of 2 g. 3β-acetoxy-14ξ-hydroxy-5-androstene-17-one in acetic anhydride, and heated 15 min. at 95-100° → 1.38 g. 3β-acetoxy-5,14-androstadien-17-one.—Other methods were not successful. A. F. St. André et al., Am. Soc. *74*, 5506 (1952).

p-Toluenesulfonic acid *TsOH*

s. 7, 891; s. a. A. Eschenmoser, J. Schreiber, and S. A. Julia, Helv. *36*, 482 (1953)

Dehydration-rearrangement ←

s. *9*, 958

Sulfuric acid *H_2SO_4*

Dehydration of alcohols CHC(OH) → C:C

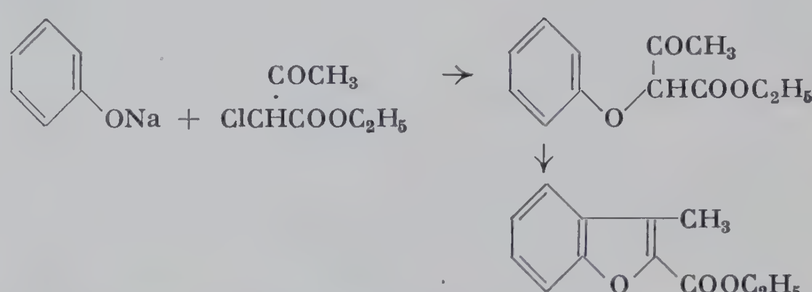
s. *5*, 627; s. a. K. W. Rosenmund and H. Herzberg, B. *87*, 1575 (1954)

Isocyclics from alcohols ○

s. *2*, 794; *4*, 832; s. a. F. E. and T. J. King, Soc. *1954*, 1373

Benzofurans
Aryl ethers

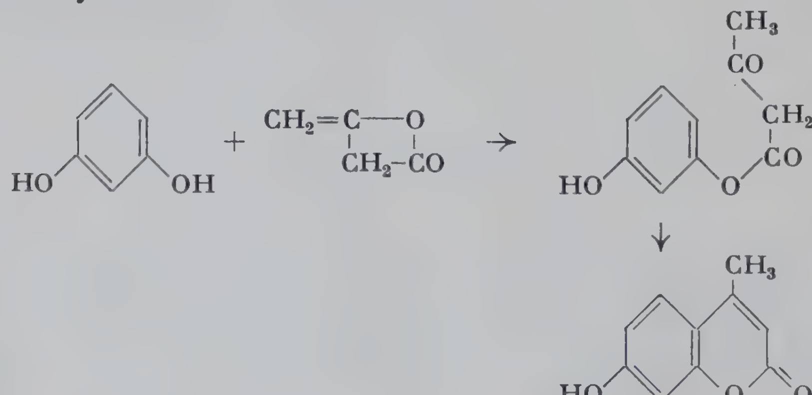
953.



Ethyl α-chloroacetoacetate added with stirring to a suspension of Na-phenolate in dry benzene at such a rate as to maintain gentle refluxing, which is continued with stirring for 4 hrs. → crude ethyl α-phenoxy-acetoacetate (Y: 85-90%) added with stirring during 1 hr. below 5° to concd. H_2SO_4, and allowed to stand in the ice bath for 1 hr. longer → ethyl 3-methylcoumarilate (startg. m. f. 159) (Y: 35-42%). W. R. Boehme, Org. Synth. *33*, 43 (1953).

Synthesis of O-heterocyclics with diketene
4-Methylcoumarins from phenols and diketene
via arylacetoacetic acid esters
O-Acetoacetylation

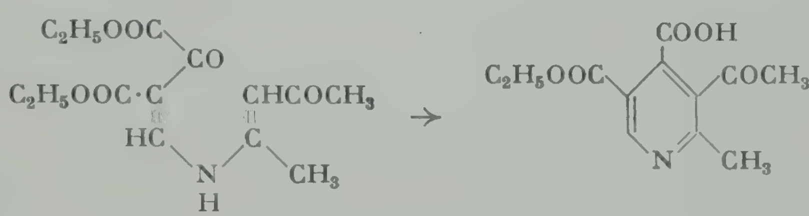
954.



Diketene added during 1 hr. to an agitated suspension of resorcinol in boiling benzene containing a little triethylamine, and heating continued for 0.5 hr. → m-hydroxyphenyl acetoacetate (Y: 99%) added during 15 min. with agitation and cooling at 70° to 98%-H_2SO_4, and kept a further 0.5 hr. at the same temp. → 7-hydroxy-4-methylcoumarin (Y: 85%). —The yields, in general, run parallel to those obtained from the Pechmann reaction (cf. Synth. Meth. *1*, 591; *2*, 673, 682). F. e. s. R. N. Lacey, Soc. *1954*, 854; O-acetoacetylation and f. O-heterocyclics s. a. other papers of this series.

Pyridine ring from enamines

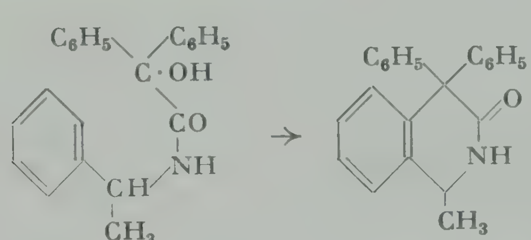
5.



97%-H_2SO_4 added to diethyl [(1-methyl-3-oxo-1-butenylamino)methylene]oxalacetate, cooled with ice to keep the temp. at ca. 50-55°, and allowed to stand 2 hrs. at room temp. after the exothermic reaction has subsided → 5-acetyl-3-carbethoxy-6-methyl-4-pyridinecarboxylic acid. Y: 70%. F. e. s. R. G. Jones, Am. Soc. *73*, 5244 (1951).

N-Heterocyclics from hydroxycarboxylic acid amides

6.

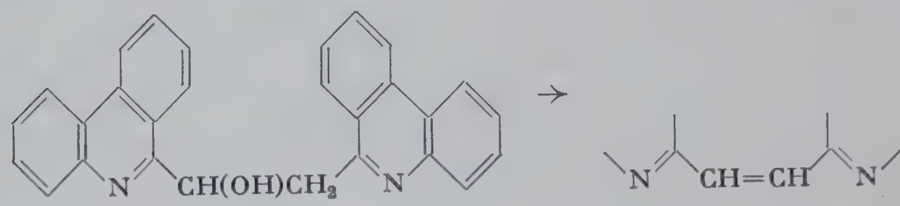


Concd. H_2SO_4 added to a soln. of N-(α-methylbenzyl)benzilamide in glacial acetic acid, and the product isolated after disappearance of a red-brown color → 1-methyl-4,4-diphenyl-3-oxo-1,2,3,4-tetrahydroisoquinoline. Y: 91.55%.—Amides of aliphatic α-hydroxyacids do not undergo this reaction, neither do the amides of α-hydroxyacids in which the carbinol C-atom carries but 1 aryl group. None of these amides give a color with H_2SO_4. F. e. s. P. A. Petyunin, Ж. *22*, 700 (1952); oxindoles with $ZnCl_2$ s. Ж. *22*, 697; C. A. *47*, 5385e,a; limitations s. a. Ж. *22*, 1187; C.A. *47*, 7490b.

Selenium dioxide *SeO_2*

Dehydration of alcohols CHC(OH) → C:C

957.



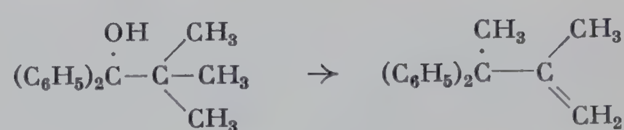
A soln. of 900 mg. 1,2-di-(6-phenanthridinyl)ethanol in dioxane containing a little water refluxed 4 hrs. with SeO_2 → 600 mg. 1,2-di-(6-phenanthridinyl)ethylene. A. G. Caldwell, Soc. *1952*, 2035.

Hydrochloric acid *HCl*

s. *6*, 862; s. a. *9*, 601; P. L. Pauson, Am. Soc. *76*, 2187 (1954)

Dehydration-rearrangement ←

958.



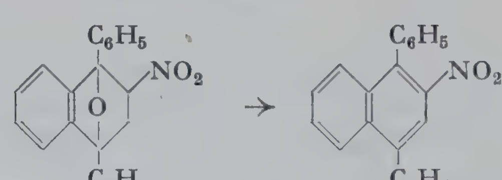
An alc. soln. of 1.7 g. 2,2-dimethyl-1,1-diphenylpropan-1-ol refluxed 3 hrs. during the passage of dry HCl-gas → 1.35 g. 2-methyl-3,3-diphenyl-1-butene. F. e., also with p-toluenesulfonic acid as reagent, s. E. J. Skerrett and D. Woodcock, Soc. *1952*, 2804.

Ethylenecarboxylic acids
from hydroxycarboxylic acid esters ←

s. *9*, 25

Aromatization
by elimination of an oxygen bridge ←

959.



1,4-Diphenyl-2-nitro-1,4-epoxy-1,2,3,4-tetrahydronaphthalene refluxed 15 min. in alcohol containing HCl → 1,4-diphenyl-2-nitronaphthalene. Y: ca. 100%. F. e. s. A. Etienne, A. Spire, and E. Toromanoff, Bl. *1952*, 750.

Via intermediates *v.i.*

Ketenes from carboxylic acids via α-bromocarboxylic acid bromides CHCOOH → C:C:O

0. $(CH_3)_2CHCOOH \rightarrow (CH_3)_2CBrCOBr \rightarrow (CH_3)_2C{=}C{=}O$

Br added dropwise with stirring to a mixture of isobutyric acid and red P, then heated 6 hrs. at 100° → α-bromoisobutyryl bromide (Y: 75-83%) added dropwise to Zn-turnings and ethyl acetate under a slow dry N_2-stream at such a rate that the ethyl acetate boils gently → dimethylketene (Y: 46-54% as a 9-10% soln. in ethyl acetate). C. W. Smith and D. G. Norton, Org. Synth. *33*, 29 (1953).

Nitrogen ↑ CC $\Uparrow$ N

Without additional reagents *w.a.r.*

Sym. α-dinitriles from ketones via sym. hydrazo- and azo-dinitriles Dimerization ←

s. *6*, 869; ring-strain determination s. Am. Soc. *75*, 2078 (1953)

Hoffmann degradation to ethylene derivatives $CH\overset{+}{N}\langle \rightarrow C{:}C$

s. *8*, 917; stereochemical specificity s. R. D. Haworth, J. McKenna, and R. G. Powell, Soc. *1953*, 1110

Potassium hydroxide/platinized asbestos ←

s. Platinized asbestos/potassium hydroxide

Sodium/ethylene glycol *Na/HOCH$_2$CH$_2$OH*

Alkaline decomposition of p-toluenesulfonylhydrazones ←

61.

p-Toluenesulfonylhydrazones give diazo compounds or products of their decomposition: olefins, sometimes with rearrangement of the carbon skeleton, triazole derivatives from bis-p-toluenesulfonylhydrazones of some 1,2-diketones.—E: Cyclohexanone-p-toluenesulfonylhydrazone refluxed 1.5 hrs. with a 1.3 *N* soln. of Na in ethylene glycol → cyclohexene. Y: ca. 100%. F. e. s. W. R. Bamford and T. S. Stevens. Soc. *1952*, 4735.

Mercuric oxide *HgO*

Acetylene derivatives from osazones $C(:N{\cdot}NH_2)C(:N{\cdot}NH_2) \rightarrow C{\vdots}C$

s. *8*, 924; s. a. A. C. Cope, D. S. Smith, and R. J. Cotter, Org. Synth. *34*, 42 (1954)

Sulfuric acid *H_2SO_4*

Fischer indole synthesis ○

s. *8*, 740, 926; s. a. V. V. Feofilaktov, Sint. Org. *2*, 98, 103 (1952); C. A. *48*, 668h, 666g.

Hydrochloric acid *HCl*

962. **with aldehyde hydrazones.** n-Butyraldehyde p-nitrophenylhydrazone dissolved in a suspension of p-nitrophenylhydrazine in concd. HCl, a layer of benzene added, stirred 3 hrs. at room temp., benzene replaced with fresh solvent for a second 3 hrs., and the crude product chromatographed → 3-ethyl-5-nitroindole. Y: 20-25%. F. e. s. E. Shaw and D. W. Woolley, Am. Soc. *75*, 1877 (1953).

Platinized asbestos/potassium hydroxide ←

Cyclopropanes from
α,β-ethyleneoxo compounds
via 2-pyrazolines

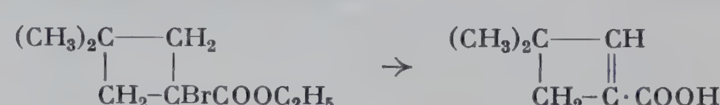
s. *8*, 927; pyrolysis with KOH and other catalysts cf. S. G. Beech, J. H. Turnbull, and W. Wilson, Soc. *1952*, 4686

Halogen ↓ CC ⇑ Hal

Potassium hydroxide/toluene *KOH*

Ethylene derivatives from halides CHHal → C:C

963.



Potassium hydroxide vigorously stirred under refluxing toluene, ethyl 1-bromo-3,3-dimethylcyclobutanecarboxylate added dropwise without external heating, which is then resumed for a further 40 min., cooled, and water added → crude 3,3-dimethylcyclobut-1-enecarboxylic acid. Y: 97%.—More conventional methods were not successful. F. e. s. A. Campbell and H. N. Rydon, Soc. *1953*, 3002.

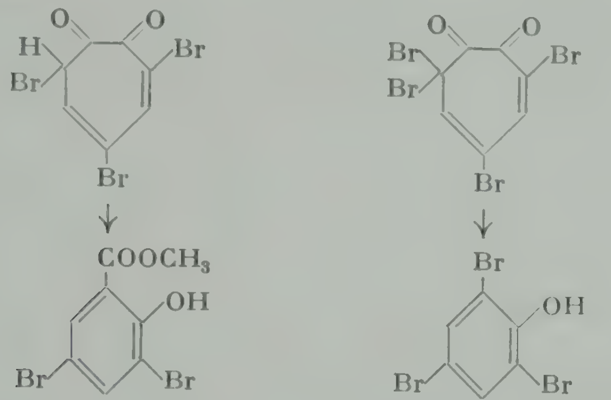
Potassium hydroxide/alcohol

964. $$CF_3CHICH_2CF_3 \rightarrow CF_3CH{=}CHCF_3$$

Ethylenehalides. 10% excess alc. 10%-KOH slowly run into a soln. of 1,1,1,4,4,4-hexafluoro-2-iodobutane at 10°, and after 20 min. allowed to warm to 25° → *trans*-1,1,1,4,4,4-hexafluoro-2-butene. Y: 95%. F. e. s. R. N. Haszeldine, Soc. *1952*, 2504; s. a. V. Prey and H. Berbalk, M. *82*, 990 (1951); also with aq. KOH s. A. L. Henne, J. W. Shepard, and E. J. Young, Am. Soc. *72*, 3577 (1950).

Benzene ring from cyclohepta-4,6-diene-1,2-diones Ring contraction ←

5.



0.5 g. 3,5,7-tribromo- | 0.3 g. 3,3,5,7-tetrabromo-

cyclohepta-4,6-diene-1,2-dione dissolved in methanol cooled with ice-salt mixture, and 3 *N* methanolic KOH added slowly with stirring →

0.3 g. methyl 3,5-dibromosalicylate. | 0.18 g. 2,4,6-tribromophenol.

H. Fernholz, E. Hartwig, and C.-J. Salfeld, A. *576*, 131 (1952).

Potassium hydroxide/quinoline

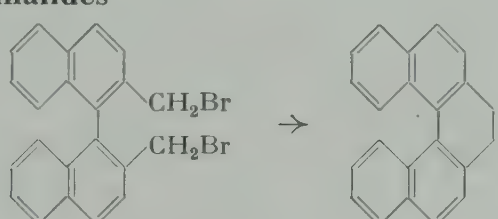
Polyaryl condensation

s. *1*, 768; s. a. E. Clar, W. Kelly, and J. W. Wright, Soc. *1954*, 1108

Phenyllithium C_6H_5Li

Isocyclics from dihalides

6.



An ethereal soln. of phenyl-Li from bromobenzene and Li added dropwise with stirring under N_2 during 15 min. to a soln. of 2.2′-di(bromomethyl)-1,1′-dinaphthyl in benzene. stirring continued 1 hr. at room temp., benzene added, and refluxed 1 hr. → 9,10-dihydro-3,4,5,6-dibenzphenanthrene. Y: 80%. E. D. Bergmann et al., Am.Soc.*73*, 5153 (1951); J. Org. Chem. *19*, 1383. 1387 (1954); cyclobutane ring from diiodides s. K. Alder and H. A. Dortmann. B. *87*, 1492 (1954); intermolecular ring closure s. W. Baker, J. F. McOmie, and W. K. Warburton. Soc. *1952*, 2991; also dimerization of halides s. E. D. Bergmann and Z. Pelchowicz, Am. Soc. *75*, 4281 (1953).

Lithium amide *$LiNH_2$*

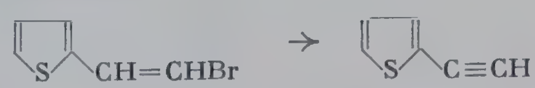
Acetylene derivatives from α,β-ethylenehalides with subsequent synthesis of acetylenealcohols CH:CHal → C⫶C

s. *9*, 736

Sodium amide/aniline *$NaNH_2/C_6H_5NH_2$*

Sensitive acetylene derivatives by dehydrohalogenation ←

967.



A soln. of 2-(2-bromovinyl)thiophene in abs. ether containing a little aniline added during 15-30 min. to $NaNH_2$ prepared from Na in the presence of $Fe(NO_3)_3$ in liq. NH_3, and stirring continued for 0.5 hr. → 2-thienylacetylene. Y: 65%. F. e. s. A. Vaitiekunas and F. F. Nord, J. Org. Chem. *19*, 902 (1954).

Potassium carbonate *K_2CO_3*

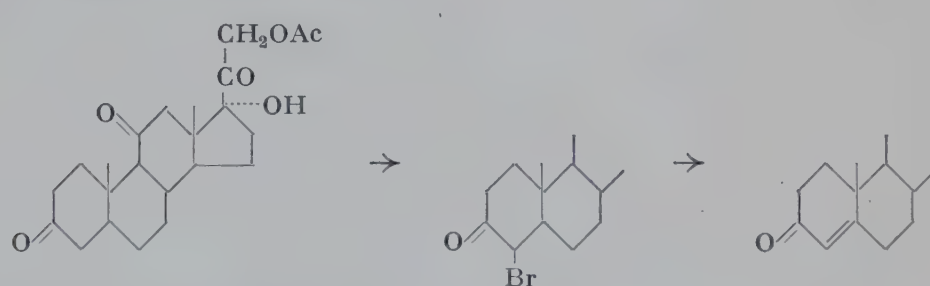
α,β-Ethylenehalides from α,β-dihalogenocarboxylic acids CHHalCHHalCOOH → CH=CHHal

s. *6*, 880; stereoisomers cf. S. J. Cristol and W. P. Norris, Am. Soc. *75*, 2645 (1953)

Lithium chloride *LiCl*

Δ^4-3-Ketosteroids via 4-halogeno-3-ketosteroids CHCHal → C:C

968.



A soln. of Br in *dimethylformamide* added during 7-9 hrs. at room temp. to a soln. of 17α-hydroxy-21-acetoxypregnane-3,11,20-trione and a little p-toluenesulfonic acid monohydrate in dimethylformamide, then water added over a 20-min. period → 4-bromo-17α-hydroxy-21-acetoxypregnane-3,11,20-trione (Y: 70-85%) dissolved with anhydrous LiCl in *dimethylformamide*, and heated 2 hrs. at 100° under N_2 → cortisone acetate (Y: 73%). F. e. s. R. P. Holysz, Am. Soc. *75*, 4432 (1953).

Aniline/sodium amide *$C_6H_5NH_2/NaNH_2$*

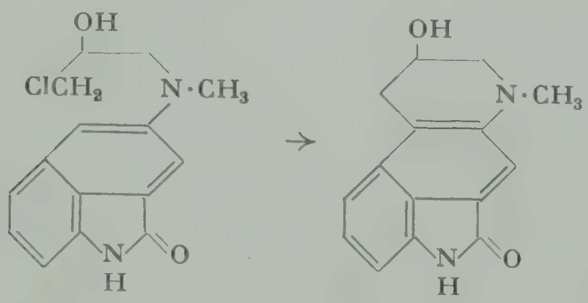
s. Sodium amide/aniline

Diethylaniline *$C_6H_5N(C_2H_5)_2$*

Dehydrobromination CHCBr → C:C

s. *9*, 619

Ring closure to N-heterocyclics ○



Startg. m. refluxed 3 hrs. in cyclohexanol containing diethylaniline → 1,2,3,4-tetrahydroquinoline derivative. Y: 75%. A. Stoll, T. Petrzilka, and J. Rutschmann, Helv. *35*, 1249 (1952).

Piperidine *$C_5H_{11}N$*

α,β-Ethylenenitriles from α-bromonitriles CHCBr → C:C

s. *9*, 899

Silver acetate *CH_3COOAg*

Ethylene derivatives from 1,2-dibromides CBrCBr → C:C

s. *9*, 928

Zinc *Zn*

s. *9*, 362

Acetylenehalides CBr:CBr → C⋮C

$$CF_3CBr{=}CBrCF_3 \rightarrow CF_3{\cdot}C{\equiv}C{\cdot}CF_3$$

2.3-Dibromo-1,1,1,4,4,4-hexafluoro-2-butene treated with Zn in abs. alcohol with vigorous stirring under reflux for 4 hrs. → 1,1,1,4,4,4-hexafluoro-2-butyne. Y: 90%. F. e. s. R. N. Haszeldine, Soc. *1952*, 2504, 3483.

Ketenes from α-halogenocarboxylic acid halides CHalCOHal → C:C:O

s. 9, 960

Zinc/sodium iodide *Zn/NaI*

Ethylene derivatives from 1,2-dibromides CBrCBr → C:C

s. 9, 603

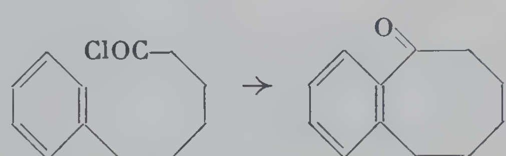
Zinc/acetic acid *Zn/CH_3COOH*

s. 9, 97

Aluminum chloride *$AlCl_3$*

Cyclic ketones from carboxylic acid chlorides Ruggli-Ziegler dilution principle ○

971.

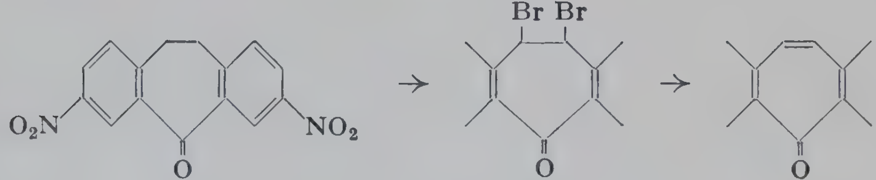


45.6 g. ε-phenylcaproyl chloride in 1250 c.c. CS_2 added dropwise through the condenser during 40 hrs. with stirring and vigorous refluxing to 100 g. $AlCl_3$ in 1750 c.c. CS_2 so that the acid chloride soln. is further diluted by the refluxing solvent → 1,2-benzo-1-cycloöcten-3-one. Y: 68%.—Intramolecular ring closure is facilitated by high dilution (Ruggli-Ziegler dilution principle). R. Huisgen and W. Rapp, B. *85*, 826 (1952).

Trimethylene glycol *$OH[CH_2]_3OH$*

Dehydrogenation via 1,2-dibromides CBrCBr → C:C

972.



2′,2″-Dinitro-2,3:6,7-dibenzocyclohepta-2,6-dien-1-one refluxed 8-10 hrs. with bromine and CCl_4, with irradiation by 4 100-W-lamps, evaporated to dryness, and the residue refluxed ¾ hr. with trimethylene glycol → 2′,2″-dinitro-2,3:6,7-dibenzocyclohepta-2,4,6-trien-1-one. Y: 83-85%. F. e. s. T. W. Campbell, R. Ginsig, and H. Schmid, Helv. *36*, 1489 (1953).

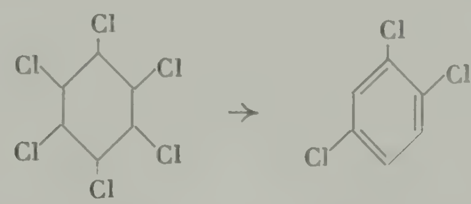
Amberlite

←

Aromatization

CHCCl → C:C

3.



A mixture of α- and β-isomers of benzene hexachloride and Amberlite IRA-400 base refluxed 30-40 min. at 240°, then distilled → 1,2,4-trichlorobenzene (startg. m. f. 306). Y: 85%. A. Galat, Am. Soc. *74*, 3890 (1952).

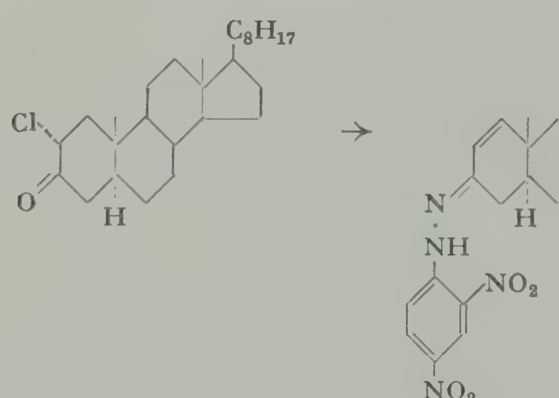
Acetic acid

CH_3COOH

Mattox-Kendall reaction
α,β-Ethylenehydrazones from α-halogenoketones

CH·CHal·CO → C:C·C:N·NHR

4.



To a hot soln. of 0.5 g. 2-chlorocholestane-3-one in glacial acetic acid added 2,4-dinitrophenylhydrazine in acetic acid, and refluxed 3 min. under N_2 → 0.57 g. Δ^1-cholestene-3-one 2,4-dinitrophenylhydrazone. F. e. s. J. J. Beereboom et al., Am. Soc. *75*, 3500 (1953).

Allyl bromide

CH_2:$CHCH_2Br$

Ethylene derivatives from bromides

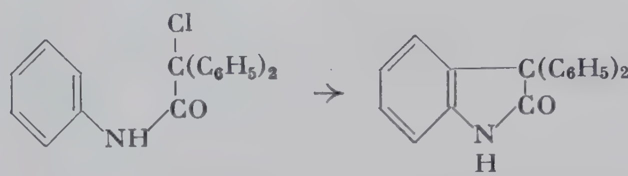
CHCBr → C:C

s. *9*, 927

Sulfuric acid *H_2SO_4*

N-Heterocyclics from halogenocarboxylic acid amides
Oxindoles

975.



Concd. H_2SO_4 added to a soln. of diphenylchloroacetanilide in glacial acetic acid, and warmed 5-10 min. at 60° until the red color disappears → 3,3-diphenyloxindole. Y: 96.7%. F. e. s. P. A. Petyunin, Ж. *22*, 975, (1952); C. A. *47*, 7489g.

Via intermediates *v.i.*

α,β-Ethyleneketones from α-halogenoketones CHCHal → C:C
Mattox-Kendall reaction

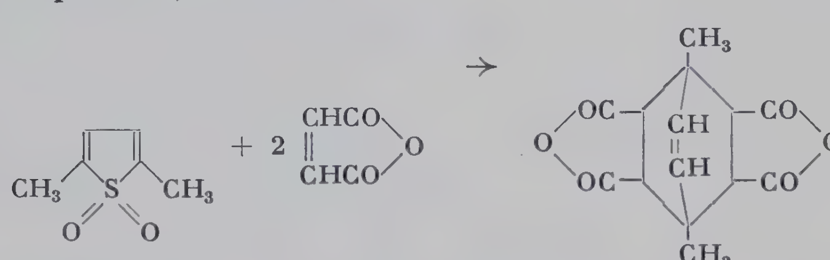
from α-bromoketones s. *6*, 891; also from α-chloroketones s. R. H. Levin et al., Am. Soc. *76*, 546 (1954)

Sulfur ↑ CC⇑S

Without additional reagents *w.a.r.*

7-Bicyclo[2.2.2]octene-2,3,5,6-tetracarboxylic acid anhydrides from thiophene 1,1-dioxides

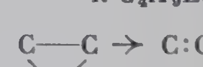
976.



2,5-Dimethylthiophene 1,1-dioxide and maleic anhydride heated 5 min. at 150° in a small tube → 1,4-dimethylbicyclo[2.2.2]oct-7-ene-2,3,5,6-tetracarboxylic acid anhydride. Y: 71%. F. e., also in benzene, s. J. L. Melles, R. *71*, 869 (1952).

n-Butyllithium *n-C_4H_9Li*

Ethylene derivatives from ethylene sulfides



s. *9*, 689

Copper *Cu*

Stilbenes from s-trithianes C

s. *9*, 677

Lead acetate *$(CH_3COO)_2Pb$*

Ethylene derivatives and mercaptans from thioethers CHC(SR) → C:C

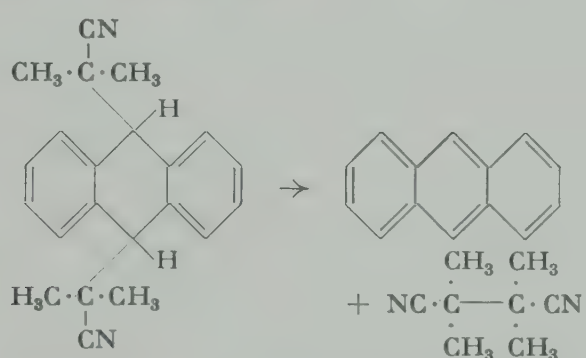
s. *9*, 655

Carbon ↑ CC ⇑ C

Without additional reagents *w.a.r.*

Thermal decomposition of subst. 9,10-dihydroanthracenes ←

77.



9.10-Di-(2′-cyano-2′-propyl)-9,10-dihydroanthracene heated 4 hrs. at 250-260° in a N_2-filled sealed tube → anthracene (Y: 92%) and tetramethyl-succinonitrile (Y: 62%). A. F. Bickel and E. C. Kooyman. R. *71*, 1137 (1952).

Reverse diene synthesis ←

s. *3*, 704; s. a. J. A. Berson and R. Swidler, Am. Soc. *76*, 2835 (1954)

Sodium hydroxide/potassium hydroxide *NaOH/KOH*

Ethylene derivatives by C-elimination ←

78.

$$(CH_3)_2C\genfrac{}{}{0pt}{}{CH_2Br}{CH_2OH} \rightarrow (CH_3)_2C{=}CH_2$$

3-Bromo-2,2-dimethyl-1-propanol added dropwise at 200° to a stirred molten mixture of KOH and NaOH → isobutylene. Y: 77%. S. Searles and M. J. Gortatowski, Am. Soc. *75*, 3030 (1953).

Potassium hydroxide *KOH*

Benzene ring ←
from cyclohepta-4,6-diene-1,2-diones

s. *9*, 965

Alkali salt ←

Ethylene derivatives from ←
salts of halogenocarboxylic acids
Degradation with loss of 1 C-atom

s. *8*, 944; cation specificity s. Am. Soc. *75*, 2698 (1953)

Barium hydroxide/iron *Ba(OH)₂/Fe*

Cyclic ketones from dicarboxylic acids ○

s. *4*, 857; s. a. H. Pommer, A. *579*, 47 (1953)

Lead tetraacetate *$(CH_3COO)_4Pb$*

Carboxylic acids from α-ketocarboxylic acids RCOCOOH → RCOOH

s. *9*, 347

Potassium hydrogen sulfate *$KHSO_4$*

Cleavage of di-tert-1,3-diols ←

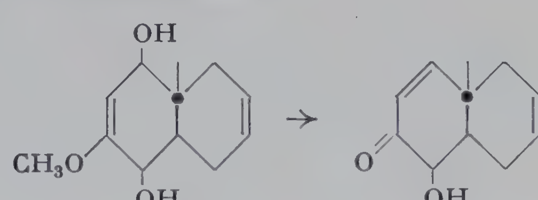
979. $$(C_6H_5)_2\underset{OH}{C}-CH_2-\underset{OH}{C}(C_6H_5)_2 \rightarrow (C_6H_5)_2C=CH_2 + OC(C_6H_5)_2$$

A mixture of 1,1,3,3-tetraphenyl-1,3-propanediol and fused $KHSO_4$ heated 3-4 hrs. at 150-180° → 1,1-diphenylethylene (Y: 56%) and benzophenone (Y: 61-79%). F. e. and methods s. J. English, Jr., and F. V. Brutcher, Jr., Am. Soc. *74*, 4279 (1952).

Sulfuric acid *H_2SO_4*

α,β-Ethyleneketones ←
from 3-alkoxy-2-ethylenealcohols

980.

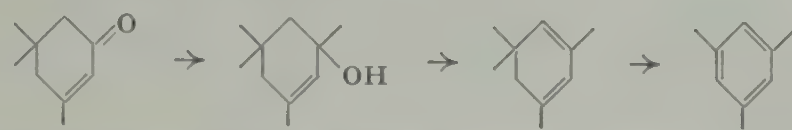


2 *N* H_2SO_4 added to a soln. of crude solid *trans*-1,4-dihydroxy-2-methoxy-10- methyl-$\Delta^{2,6}$-hexahydronaphthalene in dioxane, and allowed to stand 24 hrs. at room temp. → crude *trans*-1-hydroxy-2-keto-10-methyl-$\Delta^{3,6}$-hexahydronaphthalene. Y: 99%. F. e. s. R. B. Woodward et al., Am. Soc. *74*, 4223 (1952).

Chromium oxide-alumina *Cr_2O_3-Al_2O_3*

Synthesis of alkylbenzenes
Dehydration and aromatization ←

981.

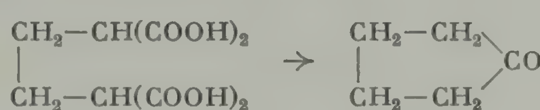


Isophorone added to ethereal methyl-MgCl, and allowed to stand several hrs. → 1,3,5,5-tetramethyl-2-cyclohexen-1-ol (Y: 83%) passed at 275° through a Pyrex-tube filled with activated alumina → 1,3,5,5-tetramethyl-1,3-cyclohexadiene (Y: ca. 90%) passed at 450-500° through a vertical tube filled with chromia-alumina catalyst (prepn. s. original) → 1,3,5-trimethylbenzene. Over-all Y: 65%. F. e. s. J. P. Ferrin et al., J. Org. Chem. *19*, 923 (1954).

Hydrobromic acid *HBr*

Cyclic ketones from polycarboxylic acids ○

982.

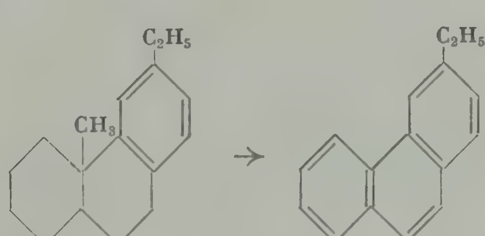


A mixture of butane-1,1,4,4-tetracarboxylic acid (prepn. s. 14) and 48%-HBr heated in an oil bath and stirred by a fine stream of N_2 which carries the steam-volatile product out continuously → cyclopentanone. Y: 79% as the 2,4-dinitrophenylhydrazone.—Lower yields are obtained when less carboxyl groups are present. Also esters and nitriles, which give free carboxyl groups in the process, can be used as startg. m. The reaction is largely specific for the formation of a 5-membered ring. F. e. s. L. Crombie, J. E. H. Hancock, and R. P. Linstead, Soc. *1953*, 3496.

Palladium-carbon *Pd-C*

Aromatization ←

983.



A mixture of 4a-methyl-6-ethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene and 5%-Pd-on-charcoal heated 12 hrs. at 300-320° → 3-ethylphenanthrene. Y: 92.3%. R. A. Barnes and R. T. Gottesman, Am. Soc. *74*, 35 (1952).

Formation of Electron Pair on Nitrogen

Elimination

Hydrogen ↑ ElN ⇑ H

Sodium hydroxide *NaOH*

Aminesulfonimides from sulfonylhydrazonium salts and reverse reaction ←

984. 

N,N,N-Trimethyl-N′-p-toluenesulfonylhydrazonium iodide triturated with 10%-NaOH → trimethylamine-p-toluenesulfonimide (Y: 87%) dissolved in water, stirred and treated slowly with HI (d. 1.50), then allowed to stand for 20 hrs. → N,N,N-trimethyl-N′-p-toluenesulfonylhydrazonium iodide (Y: 96.1%). S. Wawzonek and D. Meyer, Am. Soc. *76*, 2918 (1954).

Potassium hydroxide *KOH*

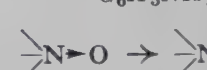
Bases from their hydrochlorides C-Aminosilanes ←

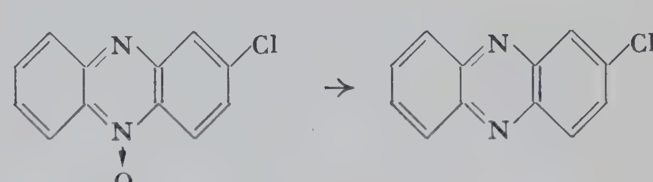
985. $(CH_3)_3SiCH_2CH_2NH_2$

Aq. β-(trimethylsilyl)ethylamine hydrochloride added dropwise under N_2 to KOH-pellets → β-trimethylsilyl)ethylamine. Y: 83.5%. F. C-aminosilanes s. L. H. Sommer and J. Rockett, Am. Soc. *73*, 5130 (1951).

Oxygen ↑ ElN ⇑ O

Aniline *$C_6H_5NH_2$*

Reduction of N-oxides 

986. 

Aniline added to 2-chlorophenazine 5-oxide, and gently refluxed 3 hrs. → 2-chlorophenazine. Y: 96%. F. e. s. I. J. Pachter and M. C. Kloetzel, Am. Soc. *74*, 971 (1952).

Lithium aluminum hydride *$LiAlH_4$*

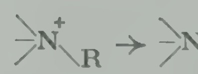
Hydrazones from azoxy compounds $\underset{\downarrow \atop O}{CH_2N}:NR \rightarrow CH:N\cdot NHR$

s. *9*, 167

Carbon ↓ ElN ⇑ C

Without additional reagents *w.a.r.*

Tert. amines from quaternary ammonium salts



s. *9*, 418; s. a. C. A. Grob and E. Renk, Helv. *37*, 1681 (1954)

Sodium hydroxide *NaOH*

Tert. amines from betaines ←

s. *9*, 217

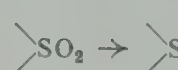
Formation of Electron Pair on Sulfur

Elimination

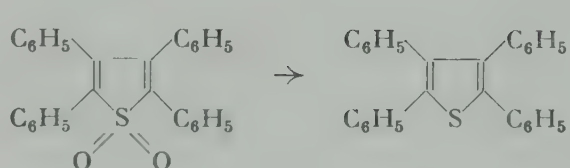
Oxygen ↓ ElS ⇑ O

Zinc/hydrochloric acid *Zn/HCl*

Thiophenes from thiophene 1,1-dioxides



87.



Zn-dust and concd. HCl added to a warm soln. of tetraphenylthiophene 1,1-dioxide in acetic acid, and the product isolated when the color has disappeared → tetraphenylthiophene. Y: 76%. F. e. s. J. L. Melles, R. *71*, 869 (1952).

Nitrogen Radicals

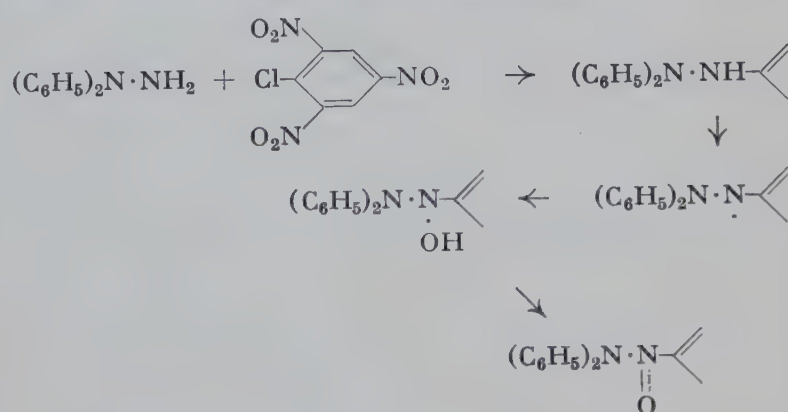
Elimination

Hydrogen ↑ **RadN ⇑ H**

Lead dioxide *PbO_2*

Oxyhydrazyl radicals from hydrazines via hydrazyl radicals and hydroxyhydrazines ←

988.



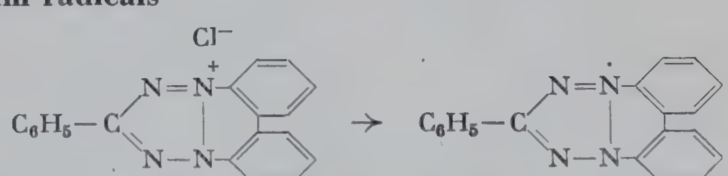
A soln. of *unsym*-diphenylhydrazine hydrochloride in abs. ethanol treated at room temp. first with $NaHCO_3$, then with picryl chloride, and gently boiled 15 min. after the CO_2-evolution has subsided → α,α-diphenyl-β-picrylhydrazine (Y: 97%) shaken 2 hrs. with PbO_2 and anhydrous Na-sulfate in benzene → α,α-diphenyl-β-picrylhydrazyl (crude Y: 95-97%) dissolved in benzene, and treated 30 min. with NO_2 gas (prepared by heating gradually a mixture of Pb-nitrate and sand to 360°) → α,α-diphenyl-β-picryl-β-hydroxyhydrazine (crude Y: 89%) allowed to react with a slurry of PbO_2 and anhydrous Na-sulfate in chloroform → α,α-diphenyl-β-picryl-β-oxyhydrazyl (Y: 77%). R. H. Poirier, E. J. Kahler, and F. Benington, J. Org. Chem. *17*, 1437 (1952).

Halogen ↑ **RadN ⇑ Hal**

Sodium stannite *Na_2SnO_2*

Tetrazolium radicals ←

989.



Aq. Na-stannite soln. (prepared from $SnCl_2$ and NaOH) added with vigorous stirring to an aq. soln. of 60 mg. 2,3-diphenylene-5-phenyl-

tetrazolium chloride and benzene, worked up after 10 min. → 40 mg. 2,3-diphenylene-5-phenyltetrazolium radical. R. Kuhn and D. Jerchel, A. *578*, 1 (1952).

Heteropolar Bond

Uptake

Addition to Oxygen — Het ⇓ O

Without additional reagents — *w.a.r.*

Trialkyl- via dialkyl-oxonium salts ←

0.

$$(CH_3)_2O + SbCl_5 \rightarrow (CH_3)_2O{\rightarrow}SbCl_5 \xrightarrow{+\ HCl} [(CH_3)_2\overset{+}{O}H]\ [SbCl_6]^- \downarrow [(CH_3)_3\overset{+}{O}]\ [SbCl_6]^-$$

$SbCl_5$ added dropwise at -70^0 to dry dimethyl ether which is vigorously agitated by a dry N_2-stream, and allowed to stand 0.5 hr. → antimony pentachloride dimethyl etherate (Y: almost 100%) dissolved at -70^0 in liq. SO_2 with stirring by a slow N_2-stream, then satd. with HCl → dimethyloxonium hexachloroantimonate (Y: almost 100%) dissolved in a minimum amount of ethylene chloride, treated with a concd. soln. of diazomethane in ethylene chloride, and the product isolated after 1.5 hrs. → trimethyloxonium hexachloroantimonate (Y: 65%). F. e. s. F. Klages and H. Meuresch, B. *85*, 863 (1952).

Addition to Nitrogen — Het ⇓ N

Without additional reagents — *w.a.r.*

Hydrochlorides $\rangle\overset{+}{N}{-}H\ Cl^-$

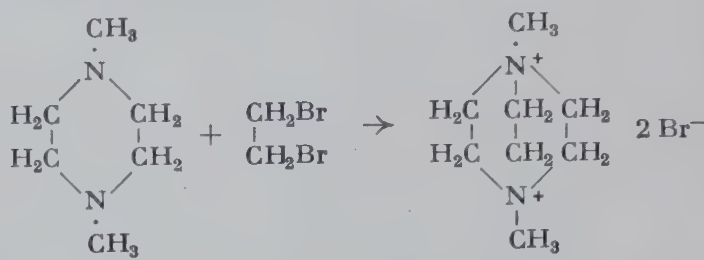
s. *2*, 829; s. a. R. B. Moffett, Org. Synth. *34*, 64 (1954)

Resolution of stereoisomers via salts ←

s. *5*, 666; s. a. B. E. Leach and J. H. Hunter, Biochem. Prep. *3*, 111 (1953); B. R. Baker et al., J. Org. Chem. *18*, 178 (1953); W. Theilacker and H.-G. Winkler, B. *87*, 690 (1954); amines with L-glutamic acid s. C. A. Grob and E. F. Jenny, Helv. *35*, 2106 (1952)

Quaternary ammonium salts
from tert. amines

991.

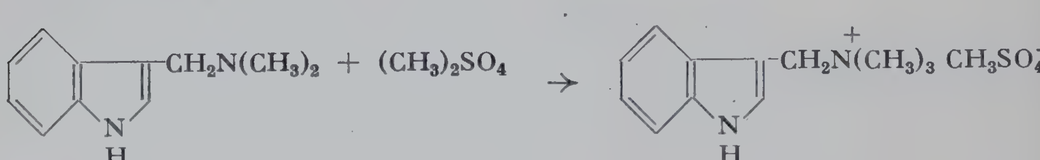


The formation of quaternary salts is faster in *polar solvents*.—E: A mixture of 1,4-dimethylpiperazine, ethylene bromide, and ethylene glycol heated slowly to 100°, and kept 1.5 hrs. at this temp. → triethylenediamine di(methobromide). Y: 70%. O. Hromatka and O. Kraupp, M. *82*, 880 (1951); s. a. W. R. Brasen and C. R. Hauser, Org. Synth. *34*, 58, 61 (1954).

Acetic acid *CH_3COOH*

Pure quaternary ammonium salts
from tert. amines
Methosulfates

992.



A soln. of gramine added dropwise at 10-15° during 0.5 hr. to a soln. of dimethyl sulfate, both in abs. tetrahydrofuran containing glacial acetic acid, and allowed to stand 3 hrs. at room temp. → trimethylskatylammonium methosulfate. Y: 80%. C. Schöpf and J. Thesing, Ang. Ch. *63*, 377 (1951).

Triphenyl phosphite methiodide *$(C_6H_5O)_3PCH_3I$*

Quaternary ammonium salts
from alcohols

993.

$$C_6H_5N(CH_3)_2 + C_2H_5OH + (C_6H_5O)_3PCH_3I \rightarrow C_6H_5\overset{+}{N}(CH_3)_2(C_2H_5)\ I^-$$

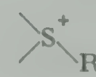
A mixture of triphenyl phosphite methiodide, abs. ethanol, and dimethylaniline heated 15 min. on a steam bath → ethyldimethylphenylammonium iodide. Y: 88%. S. R. Landauer and H. N. Rydon, Soc. *1953*, 2224.

Addition to Sulfur

Het ⇓ S

Without additional reagents *w.a.r.*

Sulfonium salts



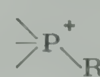
s. *2*, 836; *6*, 910; s. a. C. T. Bahner, P. P. Neblett, Jr., and H. A. Rutter, Jr., Am. Soc. *74*, 3453 (1952); also without solvent s. H. Böhme and P. Heller, B. *86*, 785 (1953)

Addition to Remaining Elements

Het ⇓ Rem

Without additional reagents *w.a.r.*

Phosphonium salts



s. *6*, 911; in benzene s. G. Wittig and U. Schöllkopf, B. *87*, 1318 (1954)

Exchange

Het ⇅

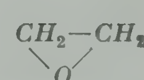
Exchange of anions of quaternary ammonium salts ←

Silver chloride *AgCl*

Chlorides from iodides

s. *9*, 949; in the presence of HCl s. H. Gilman et al., J. Org. Chem. *19*, 1067 (1954)

Ethylene oxide



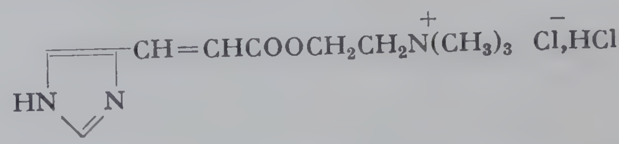
4. **New method.** Halogen anions in quaternary ammonium salts can be replaced by other anions by the use of the appropriate acid and ethylene oxide, the latter serving to remove the hydrogen halide. This procedure is particularly advantageous in the case of sensitive amino derivatives like choline.—E: Acetylcholine hydrogen sulfate. F. e. s. O. Sackur, Bl. *1952*, 796.

Amberlite

Bromides from methanesulfonates

s. *9*, 430

2,4-Diguanidinophenyl lauryl ether

995. 

Chlorides from picrates of sensitive bases. An intimate mixture of urocanyl choline dipicrate and 2,4-diguanidinophenyl lauryl ether dihydrochloride added portionwise with stirring to boiling water, boiling continued for 15 min., cooled, filtered, and the filtrate worked up → urocanyl choline chloride hydrochloride. Y: 90%. C. Pasini, A. Vercellone, and V. Erspamer, A. *578*, 6 (1952).

Other Reactions Oth

Without additional reagents *w.a.r.*

Pyridinium bromide perbromides ←

s. 8, 586; s. a. H. Baganz, B. *87*, 1373 (1954)

Index

Volume 9
(Cumulative Index, Volumes 1–5, see Volume 5, page 503;
Volumes 6–8, see Volume 8, page 387)

The subject index lists the names of the methods, types of compounds, reagents, etc. For specific compounds and for authors (when a method is not named after them) the reader may be referred to the indexes of abstract journals. Complex compounds, as those with several functional groups, are referred to under the related simpler compounds, under *special s.* E.g. aminocarboxylic acids are found under carboxylic acids. Only compounds beginning with letters other than those of the parent or main compounds are listed under this subentry, and entry numbers are omitted because they are specified when the compound is given as a main entry. Derivatives used for characterization, identification, or separation are listed under the subentry *derivatives.* Methods of synthesis for a given substance are indexed under the name of this substance and the subentry *from,* e.g. carboxylic acids from alcohols, hydrocarbons. Syntheses carried out from a particular starting material are indexed under the starting material and the subentry *startg. m. f.* (starting material for the preparation of . . .), e.g. alcohols, startg. m. f. carboxylic acids, ketones.

Classes of compounds may be designated merely by the functional group that is changed during the reaction. Ring compounds may also refer to the corresponding hydrogenated rings, unless the latter are listed specifically. If that be the case, then, as in several other cases, the *inversion* has been made use of that is customary in the indexes of Chemical Abstracts. Dihydrofurans, e.g., may be found under Furans, dihydro-. All single letters, which are separated from the name by a hyphen, are being ignored in regard to alphabetic arrangement, e.g., 'O-Acetyl derivatives' are listed under A.

Register

Band 9
(Generalregister Band 1–5 siehe Band 5, Seite 503;
Band 6–8 siehe Band 8, Seite 387)

Im alphabetischen Register finden sich als Schlagworte Methoden, Verbindungsklassen, Reagenzien u. dgl.; Einzelverbindungen und Autoren, soweit nicht eine Methode nach ihnen benannt ist, sind, wie

bisher, in den Registern der Referatenblätter zu suchen. Auf kompliziertere Verbindungen, z. B. mit mehreren funktionellen Gruppen, ist bei den entsprechenden einfacheren Verbindungen unter *special s.* (spezielle siehe) hingewiesen, z. B. bei Carbonsäuren auf Aminocarbonsäuren. Es wird hier jedoch nur auf Verbindungen hingewiesen, die einen anderen Wortanfang haben und deshalb an anderer Stelle im Register stehen. Derivate, die zur Charakterisierung, Identifizierung, oder Trennung dienen, sind unter *derivatives* aufgeführt. Methoden zur Synthese eines bestimmten Endprodukts findet man beim Schlagwort dieses Endprodukts unter *from* (aus) registriert, z. B. Carbonsäuren aus Alkoholen, Kohlenwasserstoffen. Synthesen, die sich mit einem bestimmten Ausgangsmaterial ausführen lassen, sind bei dem Schlagwort des Ausgangsmaterials unter *startg. m. f.* (Ausgangsmaterial für die Darstellung von ...) zu suchen, z. B. Alkohole, Ausg. f. Ketone, Carbonsäuren.

Die Bezeichnung der Verbindungsklassen kann sich auf funktionelle Gruppen beschränken, die bei der Reaktion verändert werden. Ringbezeichnungen können sich auch auf die entsprechenden hydrierten Ringe beziehen. Sind hydrierte Ringe aber besonders aufgeführt, dann ist bei ihnen, wie auch in einigen anderen Fällen, von der Inversion Gebrauch gemacht worden, wie sie in den Sachregistern der «Chemical Abstracts» üblich ist. Z. B. stehen Dihydrofurane unter Furane, Dihydro-. Griechische Buchstaben und Einzelbuchstaben, die vom eigentlichen Namen durch Bindestrich getrennt sind, werden bei der alphabetischen Anordnung nicht berücksichtigt, z. B. stehen «O-Acetyl-derivate» unter A.

Index

Deutscher Schlüssel zum Register (Index)

Band 1–9

	siehe unter
Dehydratisierung	Dehydration
Dehydrierung	Dehydrogenation
Diazokupplung	Diazo coupling
Dithiocarbonsäuren	Carbodithioic acids
Einführung von funktionellen Gruppen	Replacement of hydrogen
Eisen	Iron
Erdalkalien	Earths, alkaline
Erden, seltene	Earths, rare
Fluorwasserstoffsäure	Hydrogen fluoride
Gallensäurederivate	Bile acid derivatives
Glycerine	Glycerols
Halbacetale	Hemiacetals
Halogenide	Halides
Halogenwasserstoff	Hydrogen halide
Harnsäuren	Uric acids
Harnstoff	Urea
Heterocyclen	Heterocyclics
Holzkohle	Charcoal
Hydrierung	Hydrogenation
Hypohalogenite	Hypohalites
Isocyclen	Isocyclics
Isothioharnstoffe	Isothioureas
Jod	Iodine
Jod-	Iodo-
Jodwasserstoffsäure	Hydrogen iodide
Kalium	Potassium
Kern	Nucleus
Kettenverlängerung	Chain lengthening
Kohlehydrate	Carbohydrates
Kohlendioxyd	Carbon dioxide
Kohlensäure	Carbonic acid
Kohlenwasserstoffe	Hydrocarbons
Kugelmühlenreaktor	Ball mill reactor
Kunstharz-Base	Resin base
Kupfer	Copper
Kupplung	Coupling
Mangan	Manganese
Molekülverbindungen	Molecular compounds
Natrium	Sodium
Natriumäthylat	Sodium ethoxide
Oxy-	Hydroxy-
Oxydation	Oxidation
Peressigsäure	Peracetic acid
Phenyljodidchlorid	Iodobenzene dichloride
Phosphinsäuren	Phosphonic acids
Polymerisierung	Polymerization

	siehe unter
Quecksilber	Mercury
Razemate	Racemates
Reduktions-Tropfverfahren	Dropping reduction
Rhodanid	Thiocyanate
Ringerweiterung	Ring enlargement
Ringöffnung	Ring opening
Ringschluß	Ring closure
Ringverengung	Ring contraction
Salpetrigsäureester	Nitrous acid esters
Salpetersäure	Nitric acid
Schutz	Protection
Schwefel	Sulfur
Schwefelchloride	Sulfur chlorides
Schwefelwasserstoff	Hydrogen sulfide
Seitenketten	Side chains
Senföle	Isothiocyanates
Silicium	Silicon
Siliciumdioxyd	Silica
Spaltung	Cleavage
Stellungswechsel	Position shift
Stickstoff	Nitrogen
Stickstoffwasserstoffsäure	Hydrazoic acid
Sulfaminsäuren	Sulfamic acids
Sulfopersäure	Peroxymonosulfuric acid
Thiohalogenide	Sulfenylhalides
Thioharnstoff	Thiourea
Thiokohlensäuredisulfide	Disulfurdicarbothionates
Tschitschibabin	Chichibabin
Tschugaeff	Chugaeff
Umacylierung	Transacylation
Umesterung	Transesterification
Umkehrung	Inversion
Umlagerung	Rearrangement
Unterphosphorigsäure	Hypophosphorous acid
Verbindungen	Compounds
Veresterung	Esterification
Verseifung	Hydrolysis
Wanderung	Migration
Wasserstoffperoxyd	Hydrogen peroxide
Wismutverbindungen	Bismuth compounds
Wolframsäure	Tungstic acid
Zinn	Tin
Zuckersäuren	Saccharic acids

Abbreviations - Abkürzungen

abs.	absolute	absolut
alc.	alcoholic	alkoholisch
aq.	aqueous	wäßrig
ar.	aromatic	aromatisch
atm.	atmosphere(s)	Atmosphäre(n)
cf.	compare	vergleiche
concd.	concentrated	konzentriert
d.	density	Dichte
dil.	diluted	verdünnt
et al.	and others	und andere
E.	example	Beispiel
e.g.	for example	zum Beispiel
F.e.s.	Further example(s) see	weitere(s) Beispiel(e) siehe
hr(s).	hour(s)	Stunde(n)
liq.	liquid	flüssig
min.	minutes	Minuten
N	normal	normal
prepn.	preparation	Darstellung
prim.	primary	primär
s.	see	siehe
s.a.	see also	siehe auch
satd.	saturated	gesättigt
sec.	secondary	sekundär
soln.	solution	Lösung
startg. m. f.	starting material for (the preparation of...)	Ausgangsmaterial für die Darstellung von...
subst.	substituted	substituiert
sym.	symmetrical	symmetrisch
temp.	temperature(s)	Temperatur(en)
tert.	tertiary	tertiär
v.i.	via intermediates	über Zwischenprodukte
w.a.r.	without additional reagents	ohne Hilfsstoffe
Y*)	yield	Ausbeute

*) When yields are listed in parentheses, the yields so designated refer to the immediately preceding step of a multi-step reaction.

Bei mehrstufigen Synthesen beziehen sich eingeklammerte Ausbeuteangaben auf die unmittelbar vorhergehende Stufe.

Symbols - Zeichen

(on the right half of the page)		(auf der rechten Hälfte der Seite)
Electrolysis	↯	Elektrolyse
Ring closure	○	Ringschluß
Ring opening	⟳	Ringöffnung
'see title on the left half of the page'	←	«siehe Titel auf der linken Hälfte der Seite»

Journal Abbreviations - Zeitschriften-Abkürzungen

A.	Liebig's Annalen der Chemie
A. ch.	Annales de Chimie
Am. Soc.	Journal of the American Chemical Society
Ar.	Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft
Ark. Kemi	Arkiv för Kemi, Mineralogi och Geologi
B.	Chemische Berichte
Biochem.Prep.	Biochemical Preparations
Bl.	Bulletin de la Société Chimique de France
C. A.	Chemical Abstracts
C. r.	Comptes rendus (Paris)
G.	Gazzetta Chimica Italiana
H.	Hoppe Seyler's Zeitschrift für physiologische Chemie
Helv.	Helvetica Chimica Acta
J. Org. Chem.	Journal of Organic Chemistry
J. pr.	Journal für praktische Chemie
M.	Monatshefte für Chemie
Org. Synth.	Organic Syntheses
R.	Recueil des Travaux Chimiques des Pays-Bas
Ж	Journal of General Chemistry (Russia)
Soc.	Journal of the Chemical Society
Synth. Meth.	Synthetic Methods of Organic Chemistry

For other journal abbreviations see Beilstein, Handbuch der organischen Chemie or Chemical Abstracts.

Die übrigen Zeitschriften-Abkürzungen siehe Beilsteins Handbuch der organischen Chemie oder Chemical Abstracts

Systematic Survey - *Systematische Uebersicht*

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CC ↓⋂ HC	259	284	298	323
CC ↓⋂ OC	262	286	301	328
CC ↓⋂ NN	263		304	
CC ↓⋂ NC	264	292	305	332
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CC ↓⋂ CC	266	292	308	333
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CC ⇅ O	267	295	310	334
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CC ⇅ Hal	294	317	332	360
CC ⇅ S	306		345	377
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Reagents - Hilfsstoffe

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w.a.r.(heat,irradiation,↯, electric discharge)
Li, Na, Na/K, K
LiH, NaH
Na,Hg
Bases
Alkalies
Alkali hydroxide
Aq. alkali hydroxide
NaOH, KOH
Alkali in water a. alcohol
NaOH/alcohols
KOH/alcohols
Na/alcohol, NaOR, (Sodium compound)
$NaOCH_3$, $NaOC_2H_5$, $NaOC_4H_9$-n
K/alcohol, KOR
K-isopropoxide, K-tert-butoxide
n-C_4H_9Li, C_6H_5Li
$(C_6H_5)_3C{\cdot}Na$
Alkali amide
Li/liq. NH_3, Li/liq. NH_3/alcohol, $LiNH_2$, $(C_2H_5)_2NLi$, Li-methylanilide
Na/liq. NH_3, $NaNH_2$, Na-anilide
K/liq.NH_3, KNH_2
Alkali in pyridine
Na_2O_2
Na_2CO_3, $NaHCO_3$, K_2CO_3, $KHCO_3$
HCOONa
CH_3COONa, CH_3COOK
Na-citrate
Alkali cyanide, NaCN, KCN
KOCN
NaSCN, KSCN
NaN_3
$NaNO_2$, KNO_2
$NaNO_3$, KNO_3
KH_2PO_4
K-xanthate
Na_2S, Na_2S_2, Na_2S_x, NaHS
Na_2Se_x
KHS
$Na_2S_2O_3$
Na_2SO_3, K_2SO_3, $NaHSO_3$
NaF, KF, KHF_2
LiCl
Alkali iodides, NaI, KI
Alkali salts
Alkaloid-alkali salts
Na^+, K^+
NH_3
Organic bases
Resin base
Triton B, Choline, BTAB
Amines, prim., Alkylamines
Methyl-, n-Butyl-, Benzylamine
Diethylamine, Morpholine
Tert. amines, Trialkylamines, Trimethylamine, Triethylamine
Piperidine, N-Ethylpiperidine, N-Methylmorpholine
Aniline
Dialkyl-, Dimethyl-, Diethylaniline
Pyridine, Lutidine, Collidine, Quinoline
Cu, Ag, Ag-Cu, Cu,Mg
Copper oxide, Cu_2O, CuO
$Cu(OH)_2$
AgOH
$Cu{\cdot}C{\equiv}C{\cdot}C_6H_5$
Ag_2CO_3
CH_3COOAg, CF_3COOAg
Cupric carbonate, basic
$(CH_3COO)_2Cu$
Fehling solution
Copper borate
CuCN
CuSCN
Cu(I,II) sulfite
CuCl, CuBr/Mg, CuI/Mg, $CuCl_2$
Cu^+, Cu^{++}
C_6H_5COOAg
AgCN
AgN_3
$AgNO_2$
$AgNO_3$
AgF-Cu
Ag^+
CaH_2
CaO, BaO, BaO-SiO_2
$Ca(OH)_2$, $Ba(OH)_2$
$Ba(OR)_2$
CaC_2, Ca/NH_3
$(CH_3COO)_2Ba$
$CaCO_3$, $BaCO_3$
$CaSO_4$
$CaCl_2$, $BaCl_2$-C
Mg, Mg,Hg, Mg/MgI_2
Zn, Zn,Cu, Zn,Hg
Cd, Hg
HgO, MgO
$Mg(OH)_2$
$Mg(OR)_2$
RMgHal, CH_3MgI, C_6H_5MgBr
R_2NMgBr, $C_6H_5N(CH_3)$-MgBr
Zinc alkyls, Zinc alkyl halides
Organomercury compounds
$CdCO_3$
Mercury resin
$(CH_3COO)_2Hg$
$Zn(CN)_2$, $Hg(CN)_2$
$Hg(ONC)_2$ (fulminate)
$Mg(NO_3)_2$
$BeSO_4$, $MgSO_4$, $HgSO_4$
$MgCl_2$, $MgBr_2$
$ZnCl_2$, $ZnCl_2{\cdot}2NH_3$

$CdCl_2$
$HgCl/CdCO_3$
$HgHal_2$, $HgCl_2$, $HgBr_2$, HgJ_2
Mg^{++}, Ca^{++}, Zn^{++}, Hg^{++}
Al, Al,Cu, Al,Hg
$NaBH_4$, $LiBH_4$
$LiAlH_4$
$NaBH(OCH_3)_3$
$Na_2B_4O_7$
B_2O_3, HBO_2
$B(OR)_3$
Sodium perborate
Al_2O_3
TiOH
TlOR
$Al(OR)_3$
Al-isopropoxide, Al-tert-butoxide, Al-phenoxide
Al silicate
Clay, Superfiltrol
Pumice
Glass powder
$AlPO_4$/water glass
BF_3
HBF_4
$Al(Hal)_3$, $AlCl_3$, $AlBr_3$
Al^{+++}
Ce and rare earths
C
p-Cymene
CH_3OH, C_2H_5OH
Trimethylene glycol
Glycerol
$HOCH_2CH_2OCH_3$- (Methyl Cellosolve)
Methoxyacetylene
Ethylene oxide
Glucose
Hydroquinone
Oxo compounds
Formaldehyde, Benzaldehyde, Acetone
Benzophenone
Quinones
Ketene
D-Lactose hydrate
Pyruvic acid
Acetals
$(NH_4)_2CO_3$
$HCOONH_4$, CH_3COONH_4
NH_4SCN
Salts of organic bases
Acetates of organic bases
Diethylamine acetate
Tetramethylammonium acetate
Piperidinium acetate
Diazomethane
Hexamethylenetetramine
$HCONH_2$, CH_3CONH_2
$HCON(CH_3)_2$
$CO(NH_2)_2$
Phenyl isocyanate
Carbodiimides
2,4-Diguanidinophenyl lauryl ether
Fungi (Mold), Yeast
Aspergillus oryzae enzyme, Chymotrypsin, Emulsin, Hog kidney enzyme, Papain
Acetobacter suboxydans, Streptococcus faecalis
Cyanohydrins
Nitrosobenzene
Nitrosodimethylaniline
Isonitrosocyanoacetic esters
Isopropane nitronate
Nitro compounds, ar.
Nitrobenzene
Ethyl malonate
$(CH_3CO)_2O$, $(C_2H_5CO)_2O$, $(CF_3CO)_2O$
Ascaridole
Acyl peroxides
Acetyl-, Benzoyl peroxide
Ion exchange resin, Anion - -, Cation - -
Amberlite, Duolite
Dowex-50
Phenol, Resorcinol, Pyrogallol
$HCOOH$, CH_3COOH, CH_3CH_2COOH
Salicylic acid
H_2NCH_2COOH
Thioacetic acid
$ClCH_2COOH$, CCl_3COOH
$(COOH)_2$, $CH_2(COOH)_2$, Phthalic acid
CO_3^{--}
Peroxy acids
$HCOO_2H$, CH_3COO_2H
CF_3COO_2H
$C_6H_5COO_2H$, Perphthalic acid
Thiourea
Thioureas
Thiocyanates
Dimethyl sulfate
Sulfonamides
Amyl disulfide
Methyl tetrasulfide
C_6H_5IO
$C_6H_5I(OAc)_2$ (phenyl iodosoacetate)
Alkyl iodide, CH_3I, C_2H_5I
Allyl bromide
Polyhalogenoalkanes
CCl_3H, CCl_3Br
Benzotrichloride
Iodobenzene dichloride
BrCN
Bromoacetamide
Chlorourea
N-Halogenosuccinimide
N-Chloro-, N-Bromo, N-Iodosuccinimide
Bromophthalimide
Chloramin-T
Chloranil
$COCl_2$
$RCOCl$, CH_3COCl
$(COCl)_2$
C_6H_5COCl, C_6H_5COBr
$(CH_3)_2CHCHBrCOBr$
SiO_2, SiO_2-Al_2O_3
$TiO_2/HCOOH$
$SiCl_4$, $TiCl_4$
Sn
$SnCl_2$, $SnCl_4$
PbR_4
PbO, Pb_3O_4, PbO_2
$Pb(OH)_2$
$Pb(OH)_2 \cdot PbCO_3$, $PbCO_3$
$(CH_3COO)_2Pb$
$(CH_3COO)_4Pb$
$Pb(NO_3)_2$
Pb^{++}
ThO_2
Dicyanodiamide
Phenylhydrazine
$H_2N \cdot NH_2$, $C_6H_5NHNH_2$
N_3^-, HN_3

NH_2OH
Nitrogen oxides
N_2O_3, N_2O_4, N_2O_5
NH_4NO_3
Alkyl-, Butyl-, Amyl nitrite
NO_2^-
NOCl, NOBr
Alkyl nitrate
Acetyl nitrale
Nitrates
HNO_3
P
Phosphorus compounds
PH_4I
$(C_6H_5)_3P$
Phosphazo compounds
Trichlorophosphazo-sulfonyl compounds
P_2O_5
Tetraethyl pyrophosphite
$H_2PO_2^-$
H_3PO_2
Quinoline phosphate
Dialkyl chlorophosphate
H_3PO_4
P_2S_3, P_2S_5
$PHal_3$, PCl_3, PBr_3
Phenylphosphoryl dichloride
$POCl_3$, $POBr_3$
$PSCl_3$
$PHal_5$, PCl_5
As_2O_3, As_2O_5
$AsCl_3$
SbF_3, $SbCl_3$, $SbCl_5$
Bi
Bi_2O_3
BiO_3^-
Bismuth carbonate
NH_4-vanadate
V_2O_5
V_2O_5,Al_2O_3
O_2, O_3
H_2O_2
Peroxide
S
S^{--}, S_2^{--}, S_x^{--}
$(NH_4)_2S$, $(NH_4)_2S_x$
SH^-, SH_2
Na-formaldehyde-sulfoxylate
$S_2O_4^{--}$
Tetrathionate
$SO(NH_2)_2$
RSO_2NH_2
$SOCl_2$, $SOBr_2$
RSO_2Cl
Arylsulfonyl chloride
Benzene-, p-Toluene-, p-Acetylaminobenzene-sulfonyl chloride
SO_2Cl_2
SO_2
$S_2O_5^{--}$
SO_3
$(NH_4)_2SO_3$
$(NH_4)_2SO_4$
Sulfates of org. bases
Pyridine$\cdot SO_3$, Dioxane$\cdot SO_3$
$HCON(CH_3)_2\cdot SO_3$
$NaHSO_4$, $KHSO_4$, NH_4HSO_4
Sulfonates
Alkanesulfonic acids, Ethanesulfonic acid
Benzene-, p-Toluene-, m-Xylene-, Napthalene-β-sulfonic acid
Na-m-nitrobenzene-sulfonate
$HOOC\cdot CH_2\cdot SO_2H$ (sulfacetic acid)
Sulfosalicylic acid
Sulfanilic acid
$HOCH_2SO_4Na$ (hydroxy-methylenesulfonate)
$H_2NSO_3^-$, H_2NSO_3H
NH_2OSO_3H (hydroxyl-amine-O-sulfonic acid)
$ONOSO_3H$ (nitrosyl sulfate)
$ON(SO_3K)_2$ (nitrosodi-sulfonate)
H_2SO_4
H_2SO_5
S_2O_3
$(NH_4)_2S_2O_8$
$S_2O_8^{--}$
FSO_3H, $ClSO_3H$
Sulfur chlorides, S_2Cl_2, SCl_2
Se
SeO_2
Cr-Cu-C
Chromite
$CuCr_2O_4$, $CuCr_2O_4$-C
$(Ca,Cu)Cr_2O_4$, $(Ba,Cu)Cr_2O_4$
$Cr_2O_3.Al_2O_3$
MoO_x, MoO_3
CrO_4^{--}, $Cr_2O_7^{--}$, CrO_3, CrO_3-C_5H_5N
t-Butyl chromate
$CrCl_2$
CrO_2Cl_2
MoS_2
I_3^-
Halogen, Cl, Br, I
BrCN
IF_5, ICl, ICl_3, IBr
Alkyl hypochlorite, tert-C_4H_9OCl
$CF_3COOHal$
$HalO^-$, ClO^-
NaOCl, KOBr, KOI, $Ca(OCl)_2$, $Ba(OI)_2$
HOCl
ClO_3^-, BrO_3^-
$KClO_3$, $NaBrO_3$, KIO_3
HIO_3
$HClO_4$, $AgClO_4$
IO_4^-, HIO_4
Cl^-, I^-
NH_4F, NH_4Cl, NH_4I
Hydrochlorides, Hydrobromides, Hydriodides
Trimethylamine hydrochloride, Pyridine-
Acetylpyridinium chloride
Tetraethylammonium bromide
Pyridinium ethiodide
$(CH_3)_4NBr\cdot Br_2$
$C_5H_5N\cdot Br_2$
Pyridine hydrobromide-perbromide
Triphenyl phosphite methiodide
Acids/metal chlorides
Mineral acids
Hydrogen halides, HF, HCl, HBr, HI
$MnCO_3$
$(CH_3COO)_2Mn$

MnO_2
K_2MnO_4
MnO_4^-
$NaMnO_4$, $KMnO_4$, $Ba(MnO_4)_2$
Fe
Fe/Fe^{++}
FeS/Al_2O_3
$FeSO_4$
$Fe_2(SO_4)_3$
$FeCl_2$, $FeCl_3$
Fe^{+++}
$Na_3[Fe(CN)_5NH_3]$
$K_3[Fe(CN)_6]$
Co
Co/Al_2O_3
Cr_2O_3-cobalt hydrate-$CaCO_3$
Cu-Co-Cr-asbestos
$Co(CO)_4$
$(CH_3COO)_2Co$
Co nitrite
Co-polysulfide
$CoCl_2$
CoF_3
Ni
Ni-Al
Ni/Pt, $Ni/PtCl_4$
Ni,Cr_2O_3
Nickel-zinc chromite
$Ni(CO)_4$
Ni-acetylacetonate
$NiSO_4$
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Pd-$BaSO_4$
Pd-C
Pd-pumice
PdO
OsO_4
Pt
Pt-C
PtO_2
v.i.

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